Developing and Evaluating Effective Interventions to Reduce Healthcare-Associated Infection in A Resource-Limited Hospital in Thailand

Thesis

Link(s) to article on publisher's website:
http://dx.doi.org/doi:10.21954/ou.ro.0000d7f3

Developing and Evaluating Effective Interventions

to Reduce Healthcare-associated Infection

in A Resource-limited Hospital in Thailand

Maliwan Hongsuwan

Affiliated Research Centre Programme

Mahidol Oxford Tropical Medicine Research Unit

A thesis submitted for the degree of

Doctor of Philosophy

2018 Apr

Examiners

- Professor Jacqueline Reilly, Professor of Infection Prevention and Control, School of Health and Life Sciences, Glasgow Caledonian University
- Professor Alison Holmes, Professor of Infectious Diseases, Faculty of Medicine, Department of Medicine, Imperial College London

Day of the defense: 4 Oct 2017

(Blank page)

Abstract

The burden of disease due to hospital-acquired infections in developing countries is poorly quantified. Moreover, hand hygiene compliance (amongst the most effective control measures) is often low and high quality research into how to improve it is largely lacking outside high income settings.

I aimed to: I) describe the burden and trends in healthcare associated infections in Northeast Thailand; 2) investigate knowledge and beliefs amongst healthcare workers in a tertiary hospital in Northeast Thailand about hand hygiene and identify obstacles to improving it; 3) evaluate an intervention to improve hand hygiene compliance in this hospital based on World Health Organization guidelines.

To address the first aim, a retrospective study was conducted using data from 10 provincial hospitals in Northeast Thailand (2004-2010). This demonstrated a high and increasing incidence of hospital-acquired and healthcare-associated bacteraemia, an increasing proportion of extended spectrum beta-lactamase -producing isolates, and high associated mortality.

To address the second aim, a prospective study was conducted using qualitative and quantitative methods. This found that hand hygiene compliance was poor and differed markedly among categories of healthcare workers. Obstacles to good hand hygiene behaviour included intra-personal, inter-personal, and institutional factors.

The third aim was addressed with a cluster-randomized trial to evaluate a multimodal intervention. The intervention was associated with small increases in hand hygiene compliance (OR 1.12; 95% CI 1.01 to 1.24, p = 0.027), though lack of adherence to the intervention was a major problem. Larger improvements were seen in some units (obstetrics and gynecology: OR 3.96; 95% CI 1.88 to 8.31,

$p < 0.001$) and for some types of opportunities (before patient contact: OR 1.72; 95% CI 1.32 to 2.25, $p < 0.001$).

The findings show that improvements in hygiene are possible, but multiple organizational factors need to be addressed to achieve acceptable hand hygiene levels in this setting.

Acknowledgements

First of all, I would like to thank my supervisor, Dr. Ben Cooper, for your constant support and providing me several opportunities to learn and develop me to be a PhD student then a researcher. I would like to thank you Dr. Direk Limmathurotsakul for your encouragement and constant supports. My sincere is reserved for Professor Nicholas P. J. Day, main supervisor for your guidance, feedback and helpful advice in this research. I received many things during their supervision; they do not only support me on my study but also help me to overcome various obstacles, to introducing me to a network of great people.

I also would like to give thanks to Ajarn. Vanaporn Wuthiekanun, my third party monitor, for providing kind advices and supports through my PhD life, with love and encouragement whenever I feel terribly depressed. I gratefully acknowledge to Dr. Stuart Blacksell for helping me on the Open University process and documents from the beginning of my PhD program until the last day.

I would also like to thank my kind colleagues at Microbiology Ubon Ratchathani, Mahidol Oxford Tropical Medicine Research Unit (MORU), for their technical and social supports. A big thank you to Mathematical and Economic Modelling department, MORU and Infection control team at the hospital site for their help and support in conducting this research. Additionally, I would like to say thank you to all participants who volunteered to be part of this study.

Finally, I would like to thank my family and friends for their encouragement, love and support for my long road to achieving a PhD.

Contents

List of figures

List of tables

List of abbreviations

ABHR	Alcohol-based handrub
AMR	Antimicrobial resistance
BCW	Behaviour Change Wheel
CAB	Community-acquired bacteraemia
CDC	Centers for Disease Control and Prevention
CI	Confident interval
FIT	Feedback Intervention Trial
HAB	Hospital-acquired bacteraemia
HCAB	Healthcare-associated bacteraemia
HCAI	Healthcare-associated infection
HCW	Health-care worker
ICN	Infection control nurse
ICU	intensive care unit
MDRO	Multidrug resistant organism
MRSA	Methicillin-resistant *Staphylococcus aureus*
NHS	National Health Service
NHSN	National Healthcare Safety Network
NI	Nosocomial infection
NICE	National Institute for Health and Care Excellence
RCT	Randomized controlled trial
SW-RCT	Stepped wedge cluster randomized controlled trial
TDF	Theoretical domain framework
WHO	World Health Organization
WHO-5	The WHO Five Multimodal Hand Hygiene Improvement Strategy

List of Publications

Hongsuwan M, Srisamang P, Kanoksil M, Luangasanatip N, Jatapai A, Day NP, Peacock SJ, Cooper BS, Limmathurotsakul D, Increasing incidence of hospital-acquired and healthcare-associated bacteremia in northeast Thailand: a multicenter surveillance study. PLoS One, 2014. 9(10): p. e109324.

Luangasanatip N, Hongsuwan M, Limmathurotsakul D, Lubell Y, Lee AS, Harbarth S, Day NP, Graves N, Cooper BS. Comparative efficacy of hospital hand hygiene promotion interventions: a systematic review and network metaanalysis. BMJ. 2015:351:h3728.

Chapter 1

Introduction

1.1 Background

1.1.1 Healthcare-associated infection (HCAI)

A healthcare-associated infection (HCAI) can be defined as an infection occurring in a patient during their care in a hospital or other health-care facility which was not present or incubating at the time of admission to the facility.[1] This definition includes infections which are acquired in the health-care facility but which become apparent only after discharge. It also includes occupational infections among staff of the facility.

HCAIs are a major health problem in both developed and developing countries, and represent a major cause of preventable morbidity and mortality.[2-6] Although HCAIs affect 5-10% of acute-care patients in developed countries, infection rates in developing countries have consistently been found to be much higher.[2] In addition, mortality due to such infections in developing countries has been found to greatly exceed that in resource-rich settings.[2, 3, 7]

Similar to other developing countries, HCAIs in Thailand are a major health problem and an important cause of death as well as a substantial economic burden due to the cost of treatment and additional length of stay. The point prevalence rate of nosocomial infection (NI) in Thailand was reported to be 6.5% in August 2006 (based on a study of 20 hospitals involving 9,865 patients).[8] A very similar infection rate was found in the previous survey in March 2001, when the point prevalence rate of NI (based on 42 hospitals involving 18,456 patients) was 6.4%, and 13.8% of patients with NI died, 6.7% directly due to NI.[9]

Applying infection control practices from developed countries (such as patient screening and isolation) to hospitals in developing countries would require substantial investment, although this should, to some degree, be offset by reducing the expense of nosocomial infections. There is, however, evidence that selected, concerted and low-cost interventions are able to greatly reduce the incidence of HCAIs, resulting in improved patient outcomes.[10, 11] However, results from a study in a 1000-bed tertiary in the northeast of Thailand found that current hospital infection control guidelines are not fully implemented due, in part, to resource constraints.[12-14]

Low compliance to infection control measures is often reported,[15] and a recent World Health Organization (WHO) report highlighted a lack of knowledge concerning the control of HCAIs and the epidemiology of important healthcare-associated pathogens in developing countries.[16] Developing cost-effective interventions capable of reducing the burden of HCAI requires a detailed knowledge of local conditions, including infection control policies currently in place, and barriers to implementing both existing and enhanced control measures.

1.1.2 Hand hygiene

Health-care worker hand hygiene is widely believed to be the most important activity for the prevention of HCAIs.[17] But many observational studies demonstrate poor adherence by health-care workers (HCWs).[18-20] Several barriers to appropriate hand hygiene have been reported, including forgetfulness, ignorance of guidelines, insufficient time, high workload and understaffing, and lack of scientific information demonstrating impact of improved hand hygiene on hospital infection rates.[21-33]

Recently, behavioural theories have been applied to better understand the reasons for non-compliance with hand hygiene recommendations at the individual and institutional levels,[23, 28, 29, 33-35] but few studies come from developing countries.[28, 29] The theoretical domain framework (TDF) is a theory of behaviour change, which provides a useful conceptual basis for exploring and understanding the behaviour-change process and its effect on the health professionals' behaviour.[36, 37] The framework has been used to assess potential determinants of behavior change with both qualitative and quantitative measurement tools.[36, 38, 39] Ideally, the determinants of targeted behaviour should be identified before designing the intervention.[37] Developing an understanding of factors associated with the targeted behaviour is an important part the process of intervention development.[40-45] Therefore, before designing an intervention to promote hand hygiene among HCWs, factors associated with non-compliance in hand hygiene behaviour should be considered.

1.1.3 Intervention to promote hand hygiene

The WHO Guidelines on Hand Hygiene in Health Care were launched in 2009 to support healthcare facilities to improve hand hygiene and thus reduce HCAIs.[46-48] Components of an intervention package include 1) system change, 2) training/education, 3) evaluation and feedback, 4) reminders in the work place and 5) institutional safety climate. The WHO guidelines provides details of strategies to improve hand hygiene by implementing multiple actions to tackle different obstacles and behavioural barriers.[46]

Several studies have attempted to promote hand hygiene by applying WHO guidelines and have reported positive results on improving hand hygiene compliance.[49-51] But few studies come from developing countries,[49, 51] and only a few studies have evaluated the effectiveness of interventions for improving hand hygiene compliance using strong study designs, and almost all of these have been in high income countries.[50]

The major questions posed by this thesis are as follows:

1. What is the burden of hospital-acquired and healthcare-associated infection in a resource-limited hospital setting?
2. What are the barriers to improving hand hygiene compliance in a resource-limited hospital setting?
3. Is it possible to identify effective methods for improving hand hygiene compliance in resource-limited hospital settings?

1.2 Research aims

Research objectives are as follows:

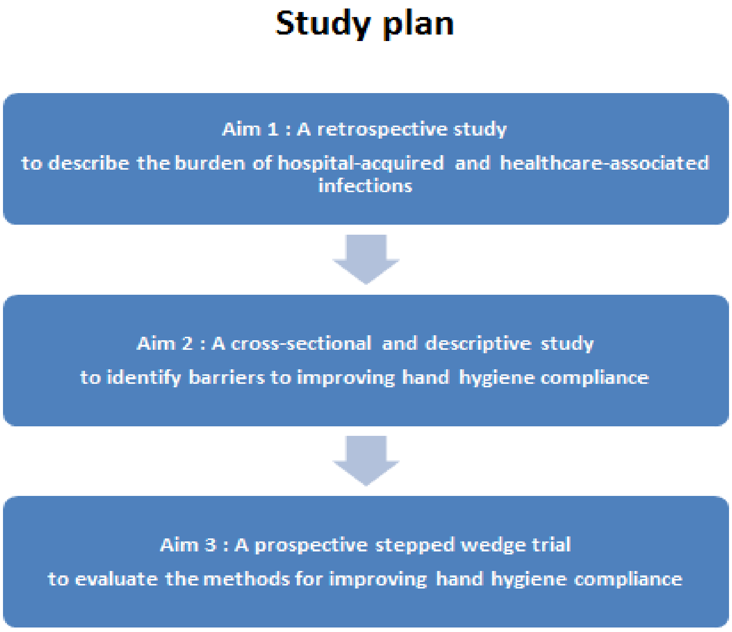
- To describe the burden of hospital-acquired and healthcare-associated infections in a resource-limited hospital setting
- To identify barriers to improving hand hygiene compliance in a resource-limited hospital setting
- To evaluate the methods for improving hand hygiene compliance in a resource-limited hospital setting

The first aim (performed in 2010) was to quantify the burden of HAIs and HCAIs. The purpose of this was to provide clear motivation for interventions to reduce this burden.

The second aim (performed in 2010-2011) was to understand the current practice regarding hand hygiene by HCWs, current levels of knowledge, and identify obstacles to improvement. The preliminary results from this aim were used to inform the intervention in the third aim, though more detailed analysis of data collected for this aim was not performed until the last year of thesis, when the intervention study had been completed. It was hoped that this more detailed analysis would help understand why the intervention had worked well in some places, but less well in others.

The third aim (conducted between 2012-2015) was to evaluate an intervention for improving hand hygiene practice among HCWs. The intervention study was developed in 2012, and actually conducted between 2013-2015.

Figure 1.1: Study framework of the thesis: "Developing and evaluating effective interventions to reduce healthcare-associated infection in a resource-limited hospital in Thailand"



1.3 Contribution of thesis

This thesis makes three contributions. The first contribution is to quantify the burden of hospital-acquired and healthcare-associated infections in a resource-limited hospital setting. The second contribution is to apply the theoretical domain framework to identify systematically the obstacles to improving hand hygiene behaviour in a resource-limited hospital, and to develop a deeper understanding of beliefs and perceptions about hand hygiene behaviour. The third contribution is to evaluate an intervention package to improve hand hygiene suitable for resource-limited hospitals.

The overall aim is to generate generalisable knowledge that is of relevance not only to other resource-constrained hospitals in Thailand but which, given the lack of methodologically sound evaluations of the impact of hand hygiene interventions in hospitals in developing countries, also has much wider international significance.

1.4 Outline of thesis

In addition to this introductory chapter, this thesis has five further chapters:

Chapter 2 is a review of the current literature on HCAI, relationship between hand hygiene and HCAIs, hand hygiene behaviour, and interventions to promote hand hygiene.

Chapter 3 addresses the first aim, quantifying the burden of hospital-acquired and healthcare-associated infections in a resource-limited hospital setting.

Chapter 4 addresses the second aim, identifying barriers to improving hand hygiene compliance in a resource-limited hospital setting.

Chapter 5 is concerned with the third aim, to evaluate an intervention intended to improve hand hygiene compliance in a resource-limited hospital setting.

Chapter 6 is a general discussion and summary of findings from this thesis. Implications of the research findings, and strengths and limitation of this thesis are considered. Future research directions are also discussed.

Chapter 2

Literature Review

2.1 Healthcare associated infection

This section will consider: i) what are healthcare associated infections (HCAIs) and what standard terminology is used; ii) transmission of HCAIs; and iii) impact of HCAIs.

2.1.1 What are healthcare-associated infections and what is the standard terminology?

In 1988, The Centers for Disease Control and Prevention (CDC) [52] classified surveillance infection data into two types, community acquired and nosocomially acquired infections, and also developed a new set of definitions of nosocomial infections for specific infection sites (e.g. urinary, pulmonary).[52]

In 2002, The World Health Organization (WHO)[53] decided that what had been called "nosocomial infection" would be referred to as "hospital-acquired infection". The definition of "hospital-acquired infection" includes infections acquired in the hospital but appearing after discharge, and also occupational infections among staff of the facility.[53]

Since 2008, the CDC[54] have used the generic term "healthcare-associated infection" instead of "nosocomial infection", modifying the new definition to "infections that patients acquire during the course of receiving treatment for other conditions within a healthcare setting". This includes infection that develops in hospital, or a systemic condition resulting from an adverse reaction to an infectious agent(s) or its toxin(s) after 48 hours of hospitalization.[54]

In 2011, the National Institute for Health and Care Excellence (NICE)[55] in the United Kingdom began publishing public health guidelines and also defined healthcare-associated infections (HCAIs) to be infections occurring as a direct result of healthcare interventions such as medical or surgical treatment, or from being in contact with a healthcare setting.[55]

Nosocomial or hospital-acquired infection therefore refers to an infection that exists during hospitalization or after discharge. The term healthcare-associated infection is used when the infection is not present before someone has been under medical care, but is present after 48 hours of hospitalization.

Hospital-acquired pathogens with multidrug resistant bacteria are frequently found in patients who have a positive blood culture within 48 hours of hospitalization,[56] which suggests community onset of the infection. Within the last 15 years some researchers have proposed a new class/definition of "healthcare-associated" infection distinct from both community-acquired and hospital-acquired infections for bloodstream infection[57-59] by considering the aetiology (such as the history of exposure to healthcare settings prior to admission) and predisposing conditions. Table 2.1 summaries these classifications of bloodstream infections by Shorr *et al*.[59]

The current study focuses on all infections that are acquired from the healthcare setting (including hospital-acquired and healthcare-associated infections). Therefore the specific term community acquired, hospital-acquired and healthcare-associated infections in this study are modified from Shorr *et al*.[59]

Table 2.1: Definition of community-acquired, hospital-acquired and healthcare-associated bacteraemias, from Shorr *et al*., 2006[59]

Category	Definition
Hospital-acquired bacteraemia (HAB)	Patients with a first positive blood culture > 2 days from admission
Healthcare-associated bacteraemia (HCAB)	Patients with a first positive blood culture within 2 days of admission and any of the following: ● Admission source indicates a transfer from another healthcare facility ● Prior hospitalization within 30 days
Community-acquired bacteraemia (CAB)	Patients who do not meet HAB or HCAB definitions and with the first positive blood culture ≤ 2 days

2.1.2 Transmission of healthcare-associated infections

HCAIs are infections that are not present in the patient at the time of admission to hospital but develop during the course of the stay in hospital.[60] There are two possible sources of the infection. The first source is the bacterial flora of the patient him or herself. This is called endogenous infection or self-infection. The second source is contact with new infective agents outside the patient. This is called exogenous infection or cross-infection.[61] While there is no clinical difference between the endogenous and exogenous infection, the distinction is important from the point of view of epidemiology and prevention.[60]

Healthcare-associated pathogens including multidrug-resistant pathogens can survive on three sources: as part of the bacterial flora of the patient, as part of the bacterial flora of the HCW, and in the environment in the healthcare setting. Some healthcare-associated pathogens, such as Meticillin resistant *Staphylococcus aureus* (MRSA), can colonise the body of a host (who might be a patient or

HCW) at several different sites.[62] Cross-transmission of healthcare-associated pathogens can occur via contaminated hands where contamination may arise through contact with other patients or contact with the environment.[47, 63]

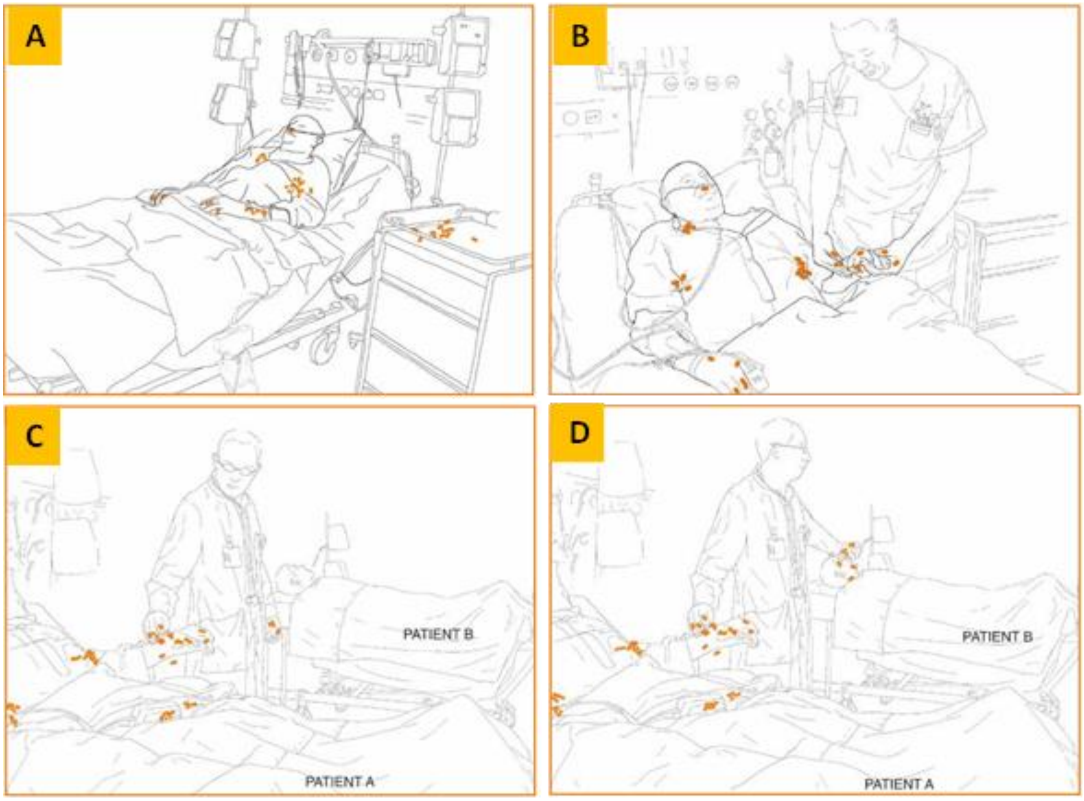
Pittet *et.al* published an evidence-based model for hand transmission during patient care that explained the sequential steps of patient-to-patient transmission of pathogens via HCWs' hands.[63] The five reported sequential steps are:

i. *organisms are present on the patient's skin or have been shed onto fomites in the patient's immediate environment;*
ii. *organisms must be transferred to HCWs' hands;*
iii. *organisms must be capable of surviving on HCWs' hands for at least several minutes;*
iv. *handwashing or hand antisepsis by the HCW must be inadequate or omitted entirely, or the agent used for hand hygiene inappropriate; and*
v. *the caregiver's contaminated hand(s) must come into direct contact with another patient or with a fomite in direct contact with the patient.*

In summary, HCW's hands can act as a vector to carry healthcare-associated pathogens from different sources (other patients, the HCW, the environment) to the patient, which can lead to colonization and subsequently infection. If this understanding is correct, it follows that some HCAIs are preventable by disinfecting HCW hands to break the chain of transmission.

Figure 2.1 presents a visualization of bacterial contamination, and cross-transmission by contaminated hands resulting from failure to clean hands of HCWs.

Figure 2.1: Bacterial contamination and cross-transmission by contaminated hands from "WHO Guidelines on Hand Hygiene in Health Care" World Health Organization, 2009,http://apps.who.int/iris/bitstream/10665/44102/1/9789241597906_eng.pdf, accessed December 2016



[A] Organisms present on patient skin or the immediate environment

[B] Organism transfer from patient to HCWs' hands

[C] Cross-transmission between patient skin and HCWs' hands

[D] Failure to cleanse hands results in between-patient cross-transmission

2.1.3 Impact of healthcare-associated infections

As mentioned in the previous section, HCAIs, also referred to as “nosocomial” or “hospital-acquired” infections, are complications of healthcare that lead to increased patient morbidity and mortality[64] and also lead to increased healthcare costs for patients, their insurers and hospitals.[1] Such infections are also an important issue for quality of care in healthcare setting.

The WHO have attempted to summarize the global burden of HCAI from several studies to highlight their importance as a public health problem, but the overall burden remains unknown , in part because of the use of different diagnostic criteria for HCAIs.[1]

The WHO data indicate that hundreds of millions of patients are affected by HCAIs worldwide each year, leading to significant mortality and financial losses for health systems.[1, 64]

In high-income countries, approximately 30% of patients in intensive care units (ICUs) are affected by at least one HCAI. In low- and middle-income countries the frequency of ICU-acquired infection is at least 2–3 fold higher than in high-income countries.[1]

HCAI rates also vary within developing countries.[3] The incidence is reported to be 5-15% of hospitalized patients and can affect 9-37% of those admitted to intensive care units.[1, 64] Several studies conducted in developing countries have reported a wide range of infection rates which are higher than in developed countries while rates of infection in some developing countries, such as Thailand, are not significantly different from developed countries. For instance, a prevalence survey conducted in Thailand in 1988, 1992, 2001 and 2006, shows that HCAIs rates were 11.7%, 7.4%, 6.4% and 6.5 %, respectively,[8] while in some parts of Asia and South Africa rates were higher than 40%.[3]

The difficulty of comparing the reported burden of HCAI in different countries was also addressed in a systematic review on HCAI in developing counties.[3] The main problems come from three key points: the first is uniformity of the definition, the second is that data may not be representative of the national level (most of the results often come from a single hospital or single ward), and the last is that there are few results from developing countries. Improving surveillance of infection in developing countries is needed to better quantify the burden of HCAI.

In summary, HCAIs can result in major costs to patients and the healthcare system, with high impact on patient safety. However, there have been few studies to quantify the burden of HCAI in developing countries. The use of methods to better understand the current situation of HCAI should be considered as one part of infection control in developing countries and given high priority.

2.2 Infection prevention and control

This section reviews infection prevention and control measures that can impact on HCAI. There are four parts: i) aims of infection control, ii) infection control guidelines, iii) standard precautions, and iv) surveillance of HCAI.

2.2.1 Aim of Infection control

Infection control is concerned with preventing HCAI, a sub-discipline of epidemiology. Infection control covers the following functions:

i. prevention (e.g. via hand hygiene/hand washing, cleaning/disinfection/sterilization, vaccination),
ii. monitoring/investigation of suspected outbreaks within a health-care setting
iii. intervention i.e. taking action to stop ongoing outbreaks.

2.2.2 Infection control guidelines

Infection control guidelines are the protocols for healthcare practitioners to standardise procedures to help stop the spread of infection. Many guidelines for infection prevention and control are generated and maintained by different organizations around the world such as the Centers for Disease Prevention and Control and the National Healthcare Safety Network (CDC/NHSN),[65] the National Health Service (NHS) hospitals in England,[66] the NICE,[67] and the WHO.[68]

In Thailand, in 1982, the Ministry of Public Health initiated nosocomial infection (NI) controls through infection control guidelines based on the CDC/NHSN guidelines.[69] Implementation of these guideline was tested in participants from 20 hospitals,[69] aiming to assess the quality of NI control. The research found that the knowledge, skill and time available for infection control of infection control nurses (ICNs) needed to be improved. Surveillance methods of NI were considered to be not appropriate in many hospitals.[69] The main problems and obstacles for implementation of NI control were the lack of support from administrators and the lack of the ICN post.[70] NI control in regional and provincial hospitals in Thailand needs more support from administrators and more co-operation from medical personnel.[71] Currently in Thailand, local hospital-specific guidelines are generated based upon each hospital's policy and details of the hospital setting, aiming to develop and implement best practice accounting for local conditions. For example, a university teaching hospital in the northern part of Thailand has developed hand hygiene guidelines as a part of infection control guidelines.[72] These infection control guideline for the hospital were derived from the infection control guidelines of the CDC/NHSN,[69] but with some adaptations to make them suitable for current policy and current practice within the hospital.

In summary, infection control guidelines are important tools to prevent and control HCAI and good infection control depends on the cooperation of all staff. Failure to implement infection control guidelines can lead to increased rates of HCAIs.

2.2.3 Standard Precautions

Standard Precautions aim to protect both staff and patients from infection and apply to all patient care, regardless of confirmed or suspected infection status of the patient, in any setting where healthcare is delivered.[73] The standard precautions include: 1) hand hygiene, 2) use of personal protective equipment (e.g., gloves, gowns, masks), 3) safe injection practices, 4) safe handling of potentially contaminated equipment or surfaces in the patient environment, and 5) respiratory hygiene.[73]

In summary, infection control measures are most effective when Standard Precautions in health care setting are applied because undiagnosed or asymptomatic infection is common. Good hand hygiene practice is an essential component of these precautions and considered as one standard part of infection prevention practice.

2.2.4 Surveillance of healthcare-associated infection

Surveillance is defined as "*the systematic, on-going collection, collation and analysis of data with timely dissemination of information to those who require it in order to take action*".[74, 75] Such actions are thought to commonly underpin improvements in prevention or control of HCAIs.

Surveillance for HCAIs is normally performed by trained infection prevention and control professionals or hospital epidemiologists. Surveillance, as part of infection prevention and control programs in health care facilities, allows detection of unusually high rates of infection and trends over time.[75] There are two types of measures commonly used as outcome indicators in surveillance: process measures (HCWs' compliance with hand hygiene) and indicators of adverse events e.g. incidence of healthcare-associated Meticillin-resistant *Staphylococcus aureus* (MRSA) bacteraemia.[27] Apisarnthanarak *et al.* , recently reviewed the role of infection prevention and control in Asia and highlighted the need for quality improvement for hospitals in Asian-Pacific countries.[76]

Interpretation of HCAI rates can identify areas where improvements to infection prevention and control practices are needed, or evaluate where preventive interventions have been effective in reducing the risk of infection. Because health care settings will have differing priorities for surveillance and resources available to them, case finding may vary from facility to facility.

In summary, many HCAIs are thought to be preventable though implementation of the best infection prevention and control practices. These practices include two key types of surveillance: i) surveillance of HCAI as an outcome measure, and surveillance on the rate of hand hygiene compliance as a process measure. This surveillance facilitates the delivery of high quality health care for patients and a safe working environment for HCWs.

2.3 Hand hygiene

As described earlier, HCWs' hands play a key role in the transfer healthcare-associated pathogens to patients. This section provides information on hand hygiene, and consists of three parts: i) relationship between hand hygiene and HCAI, ii) hand hygiene practice among HCWs, and iii) factors influencing adherence to recommended hand hygiene practices.

2.3.1 Relationship between hand hygiene and healthcare associated infection

Hand hygiene practices among HCWs were first recognized as an effective tool to reduce maternal mortality in the late 1840's in a Vienna hospital by Dr. Ignaz Semmelweis.[77] Since then, the importance of hand hygiene in reducing the number of HCAIs has been highlighted in many studies including observational studies, experimental studies and systematic reviews. An overview of this work is given below.

The WHO reported that at least 20 hospital-based studies of the impact of hand hygiene on the risk of HCAI were published between 1975 and June 2008.[78] Overall, they considered this to provide convincing evidence that improved hand hygiene through multimodal implementation strategies can reduce HCAI rates.[78] Despite study limitations, most reports showed a temporal relation between improved hand hygiene practices and reduced infection and cross-transmission rates.[78]

The WHO Clean Care is Safer Care team has evaluated the available evidence about the impact of hand hygiene improvement interventions to reduce transmission and/or infections by multidrug resistant organisms (MDROs) by conducting a systematic literature review from 1980 to 2013.[79] Strong evidence from this review emphasized that hand hygiene was used as the main intervention and a significant improvement in hand hygiene compliance and/or increased alcohol-based handrub (ABHR) consumption were achieved, and such improvements were associated with substantial decreases in MDRO infections and/or colonization rates, mainly for MRSA.[79] The effectiveness of hand hygiene by using ABHR was also emphasized in a randomized control trial to evaluate different guidance for hand hygiene (comparing the WHO's 6-step and the CDC's 3-step hand hygiene techniques), which provided the first evidence in clinical practice that the 6-step technique was microbiologically more effective at reducing the median log^{10} bacterial count than the 3-step technique.[80] Linking improved compliance to clinical outcomes such as number of infections prevented would provide more direct evidence about value of such interventions.[81] Some gaps and key areas where more research is needed were also identified. For example, the systematic review of the effectiveness of hand hygiene interventions[82] reported that the majority of studies came from in high-income countries and, despite limited direct evidence in hospital settings, clinical or microbiological outcomes are consistent with substantial reductions in infections for some pathogens, such as MRSA.[83] High quality surveillance data on antimicrobial resistance (AMR) and better assessments of the impact of interventions based on hand hygiene promotion activities are urgently needed from low- to- middle income countries.

In summary, promoting hand hygiene practice among HCWs has been found to be associated with significant reductions in the number of HCAIs and MDRO infections and/or colonisation rates.

2.3.2 Hand hygiene practice among healthcare worker

As described in the previous section, hand hygiene is considered to be a key measure in preventing HCAI and the spread of antimicrobial resistance in hospital settings. However, it has also been shown that HCWs encounter difficulties in complying with hand hygiene indications at different levels.

The summary of hand hygiene behaviour from the WHO noted that insufficient or very low compliance rates have been reported from both developed and developing countries, with mean baseline rates ranging from 5% to 89% and an overall average of 38.7%.[78] Hand hygiene performance varies according to work intensity and several other factors in hospitals.[78]

In summary, although many countries have guidelines regarding hand hygiene for healthcare settings, overall compliance among HCWs remains poor. Most of the studies in this summary represent single sites/single wards (such as ICU, medical ward), and the majority of the data come from developed countries. More work is needed to address compliance among HCWs in developing countries. Reducing HCAIs requires that HCWs take responsibility for ensuring that hand hygiene becomes a part of routine patient care.

Hand hygiene practice among healthcare workers in Thailand

In 2003, a quasi-experimental-time series study aimed to identify the impact of a promotion programme (including a training sessions, regular performance feedback, poster displays, provision of bedside alcohol-based handrub solution, and the distribution of individual bottles of alcohol-based hand rub) on hand hygiene practices in 26 nursing personnel and its effect on nosocomial infection rates in a neonatal ICU of a university hospital. After implementing a hand hygiene promotion programme, compliance with hand hygiene among nursing personnel improved significantly from

6.3% before the programme to 81.2% after 7 months of the programme. The compliance rate did not correlate with the intensity of patient care. The nosocomial infection rate did not decrease after the intervention, possibly because of the multifactorial nature of infections (or possibly reflecting lack of statistical power).[72]

In 2004, an observational study from 8 wards, in a 750-bed university hospital reported that the average compliance by direct observation was 24.1% (95% confidence interval [CI] = 20.5-27.9) ranging from 17.6 % to 80.0%, and the compliance rates differed between healthcare professionals and between wards.[84]

In 2005, a cross-sectional survey aimed to determine the baseline compliance regarding hand hygiene of HCWs and visitors in ICUs at King Chulalongkorn Memorial Hospital. Overall hand-hygiene compliance obtained from this observational study was less than 50% and differed markedly among various professional categories of HCWs and visitors. The best compliance was observed in nursing students with 100% adherence, which was better than that of the nurses (71.9%) and nursing assistants (63.9%), while the adherence of the physician group was poor (14.3%).[85]

In 2012, a quasi-experimental study aimed to evaluate behavioral-based interventions to improve hand hygiene among HCWs in 6 ICUs at a tertiary care center. Computer-generated randomization of 6 ICUs was to 1 of 3 strategies: hand hygiene education by infection control division every 3 months (S1; n = 2 units), intensified hand hygiene interventions (S2; n = 2 units), or intensified hand hygiene interventions plus increased availability of alcohol-based handrub throughout the unit (S3; n = 2 units). Intensified hand hygiene education included monthly education that emphasized hand hygiene adherence and impact on patient safety, as well as weekly workgroup discussions exploring reasons for not performing hand hygiene among HCWs with different behaviors. These discussions aimed to promote incremental commitment to the five moments for hand hygiene. Observation of hand hygiene practice amongst HCWs was based on the WHO five moments for hand hygiene recommendations. Compared with the pre-intervention period, overall post-intervention hand hygiene adherence improved in HCWs assigned to S2 (65% vs. 85%; P=0.02) and S3 (66% vs. 95%; P=0.005) but not S1 (68% vs. 71%; P=0.84). Improvement in hand hygiene adherence was demonstrated among HCWs who reported lower stages of hand hygiene commitment in S2 (21% vs. 84%; P<0.001) and S3 (24% vs. 89%; P<0.001) and in HCWs who self-reported higher stages of commitment in S3 (78% vs. 96%; P<0.001). The study concluded that HCW hand hygiene programs may benefit from different tailored strategies to promote sustained hand hygiene adherence.[86]

In summary, a few studies that have reported hand hygiene compliance among HCWs in Thailand have been published. Data come from university and tertiary hospitals, and all of the data are not hospital wide. A wide range of hand hygiene compliance has been currently found in Thailand, ranging from 6% to 96 %, but all reporting hand hygiene compliance improving after implementing interventions, particularly with the behavioral-based interventions.

2.3.3 Factors influencing adherence to recommended hand hygiene practices

Factors influencing hand hygiene practices have been summarized by the WHO Guidelines on Hand Hygiene in Health Care[78] in Appendix A.1, which classified these factors into three groups: i) observed risk factors, ii) self-reported factors, and iii) perceived barriers.

Pittet and Boyce also classified factors associated with non-compliance with hand hygiene into three levels:[87]

i. *individual level; including lack of education / experience, lack of knowledge of guidelines, being a refractory non-complier*
ii. *group level; including lack of education / lack of performance feedback on hand hygiene adherence, high workload, downsizing / understaffing, lack of encouragement / role model from key staff*

iii. *institutional level; lack of existing guidelines (written), lack of available / suitable hand-hygiene agents, lack of skin care promotion / agent, lack of hand hygiene facilities, lack of culture / tradition of compliance, lack of administrative leadership / sanction / rewarding/ support*

In Thailand, few studies have addressed factors associated with non-compliance. A cross-sectional survey in a questionnaire-based study aimed to assess the attitudes and beliefs regarding hand hygiene of HCWs and visitors in ICUs at King Chulalongkorn Memorial Hospital.[85] It found similar reasons for non-compliance as those outlined in the WHO report.[78] These included patient needs perceived as a priority, forgetfulness, and skin irritation by hand-hygiene agents. Subjects believed they could improve their compliance by multiple strategies including: making available hand-hygiene agents less likely to cause irritation, information of current NI rates, and easily accessed hand-hygiene supplies. The majority of the subjects claimed to know correct techniques of hand-hygiene. Handwashing with medicated soap was perceived to be the best means of hand decontamination.[85]

In summary, factors of non-compliance come from several levels of the hospital setting. It is important to address these before designing an intervention to improve hand hygiene. Psychological aspects such as attitude or beliefs regarding hand hygiene guidelines need to be considered as potentially important factors of non-compliance as well.

2.4 Behaviour change

Behaviour change is the key to improving healthcare and health outcomes[88] in particular for HCWs' behaviour. This section aims to review behavioural considerations important for understanding and improving hand hygiene behaviour amongst HCWs. This part reviews three topics: i) behavioural considerations for hand hygiene, ii) what is a behaviour change intervention?, and iii) applying behaviour change theory to improve hand hygiene behaviour.

2.4.1 Behavioural consideration on hand hygiene

The WHO's *Guidelines on Hand Hygiene in Health Care (published in 2009)* considered behavioral aspects of hand-hygiene.[89] The report emphasized that such behavioural change dynamics are complex and multi-faceted, but are of vital importance when designing hand hygiene improvement strategies. A theory-based model to explain human behaviour was presented. This classified relevant factors on the basis of being directed at the individual (intrapersonal), interpersonal, or community levels.[89] Intrapersonal factors are individual characteristics, such as knowledge, attitudes, beliefs and personality traits, that influence behaviour.[89] Interpersonal factors include groups who provide social identity, support and role definition. These include family, friends and peers.[89] Community factors are social norms and networks that exist between individuals, groups and organizations. In a hospital setting, the relevant community level would often be the ward.[89]

Whitby *et al.*[90] applied social psychology in an attempt to understand and explain behavioural patterns of hand hygiene behaviour. This behaviour has been shown to vary substantially among HCWs within the same hospital or ward, indicating that both individual and community influences play a role in determining this behaviour.[90]

In summary, the WHO classified factors affecting hand hygiene behavior into three levels: intrapersonal, interpersonal, and community factors. A similar classification was used by Michie *et al*.[42] These different levels of factors affecting hand hygiene need to be systematically addressed for individual settings when designing interventions.

2.4.2 What is a behaviour change intervention?

'Behaviour change interventions' can be defined as "coordinated sets of activities designed to change specified behaviour patterns".[37] Improving the implementation of evidence-based practice requires effective behaviour change interventions. An appropriate method for characterising interventions and linking them to an analysis of the targeted behaviour can help the process of designing effective interventions.[37]

The Behaviour Change Wheel's COM-B system

The Behaviour Change Wheel (BCW) approach[91] is underpinned by a causal analysis of behaviour. It starts with the question: 'What conditions internal to individuals and in their social and physical environment need to be in place for a specified behavioural target to be achieved?' The 'intervention mapping' approach, in contrast, starts with the question: 'What factors in the present population at the present time underlie variation in the behavioural parameter?' The BCW approach draws from a single theory of motivation in context that predicts what aspects of the motivational system need to be influenced and in what ways do they need to be influenced to achieve a specified behavioural change. In contrast the 'intervention mapping' approach is based on a number of different theoretical approaches each of which addresses different aspects of the behaviour.[91]

Michie *et al.* summarized a new method for characterizing and designing behaviour change interventions is called the 'COM-B' system.[37] This system is considered as a 'behaviour system', where system components interact to generate behaviour. Capability is defined as "the individual's psychological and physical capacity to engage in the activity concerned"; having the necessary knowledge and skills is one component of capability. Motivation can be defined as "all those brain processes that energize and direct behaviour, not just goals and conscious decision-making". Motivation includes "habitual processes, emotional responding, as well as analytical decision-making". Opportunity is defined as "all the factors that lie outside the individual that make the behaviour possible or prompt it".[37] (Table 2.3)

Table 2.2: Mapping of the Behaviour Change Wheel's COM-B system to the TDF Domains, from Cane *et al.,* 2012.[88]

COM-B component	TDF Domain	
Capability	Psychological	Knowledge
		Skills
		Memory, Attention and Decision
		Behavioural Regulation
	Physical	Skills
Opportunity	Social	Social Influences
	Physical	Environmental Context and
Motivation	Reflective	Social/Professional Role &
		Beliefs about Capabilities
		Optimism
		Beliefs about Consequences
		Intentions
		Goals
	Automatic	Social/Professional Role &
		Optimism
		Reinforcement
		Emotion

The theoretical domain frameworks

The Theoretical Domains Framework (TDF) is an "integrative framework of theories of behaviour change".[92] This framework aims to "simplify and integrate a plethora of behaviour change theories and make theory more accessible to, and usable by, other disciplines".[88] The TDF consists of fourteen domains which cover different aspects of behaviour. (Table 2.4)

Table 2.3: Domains in the theoretical domains framework, from Cane *et al.,* 2012.[88]

Theoretical Domain	**Definition[88]**
Knowledge	An awareness of the existence of something
Skills	An ability or proficiency acquired through practice
Social/Professional Role and Identity	A coherent set of behaviors and displayed personal qualities of an individual in a social or work setting
Beliefs about capabilities	Acceptance of truth, reality or validity about an ability, talent or facility that person can put to constructive use
Optimism	The confidence that things will happen for the best or that desired goals will be attained
Beliefs about consequence	Acceptance of truth, reality or validity about outcomes of behavior in a given situation
Reinforcement	Increasing of probability of response by arranging a dependent relationship, or contingency, between the response and a given stimulus
Intentions	A conscious decision to perform a behavior or a resolve to act in a certain way
Goals	Mental representations of outcomes or end states that an individual wants to achieve
Memory, attention and decision processes	The ability to retain information, focus selectively on aspects of the environment and choose between two or more alternatives
Environmental context and resource	Any circumstance of a person's situation or environment that discourages or encourages the development of skills and abilities, independence, social competence, and adaptive behavior
Social influences	Those interpersonal processes that can cause individuals to change their thoughts, feelings or behaviors

Table 2.3: Domains in the theoretical domains framework, from Cane *et al.,* 2012.[88] (cont.)

Theoretical Domain	**Definition[88]**
Emotion	A complex reaction pattern, involving experiential, behavioral and physiological elements, by which the individual attempts to deal with a personally significant matter or event
Behavioral regulation	Anything aimed at managing or changing objectively observed or measured actions

This framework has been used to explain implementation problems and inform implementation intervention in many healthcare systems, including applications to hand hygiene.[35, 93] Most of this research has used interviews and focus groups to provide details of factors related to behaviour change.

In recent years, there has been a lot of interest in using the TDF for changing clinical practice, as it represents a unifying theoretical framework to identify systematically the key aspects behavioural change including intrapersonal (individual), interpersonal, institutional and community factors.[42] (Table 2.5)

Use of the COM-B may help identify those TDF domains[42] which are likely to be important in changing behaviour (Table 2.3). The advantage of this type of behavioural analysis is that "intervention designers can be selective about the domains they investigate to inform the nature of the intervention".[42]

Table 2.4: Constructs in four theoretical domains, illustrating individual, team, and organizational levels based on construct allocations, from Michie *et al.*, 2005.[42]

Domain	**Level**		
	Individual	**Team**	**Organizational**
Environmental Context and Resources	Environmental stressors Person × environment interaction	Environmental stressors	Resources/material resources (availability and management)
Social Influences	Social support Social pressure	Leadership Social comparisons	Organizational climate/culture Change management
Social/Professional Role and Identity	Identity Professional identity	Professional boundaries/role Group/social identity	Organizational commitment
Behavioural Regulation	Goal/target setting Self-monitoring	Goal/target setting Self-monitoring	Goal/target setting Barriers and facilitators

2.4.3 Applying behaviour change theory to improve hand hygiene behaviour

In recently published research, behaviour change theory has been formally applied to address two key aspects of hand hygiene behaviour: firstly, in addressing key determinants of hand hygiene when designing the initial intervention, and secondly in the phase of implementing the intention.

Designing the intervention

Suggestions for the steps needed to develop the behaviour change intervention by using the TDF were reviewed by Frech *et al.*[94] This produced a four-step approach to guide the choice of the most appropriate components of an implementation intervention (Table 2.6).

The Medical Research Council guidance in developing and evaluating complex intervention also described key elements in the development and evaluation process, which considered identifying or developing theory as key step.[95]

For hand hygiene behaviour, factors that influence hand hygiene compliance among HCWs have been addressed in several studies using qualitative methods.[96-99]

Important advantages (protection of patient and self), disadvantages (time, hand damage), referents (supportive: patients, colleagues; unsupportive: some doctors), barriers (being too busy, emergency situations), and facilitators (accessibility of sinks/products, training, reminders) were identified among Australian hospital-based nurses.[96] It was argued that interventions to improve nurses' hand hygiene practice across the five moments needed to "focus on individual strategies to combat distraction from other duties, peer-based initiatives to foster a sense of shared responsibility, and management-driven solutions to tackle staffing and resource issues".[96]

A number of key determinants that physicians believe influence whether or not and when they practice hand hygiene have been addressed. This has helped to identify potential individual, team, and organization targets for behavior change interventions.[98] Semi-structured interviews based on the 14 TDFs of a behaviour change framework have been employed to explain health-related behaviour change that influences physician hand hygiene compliance. This study identified nine relevant domains influencing hand hygiene behaviour including "knowledge"; "skills"; "beliefs about capabilities"; "beliefs about consequences"; "goals"; "memory, attention, and decision processes"; "environmental context and resources"; "social professional role and identity"; and "social influences".[98]

Consideration of HCWs' "real-time" explanations for noncompliance identified "Memory/ Attention/Decision Making" and "Knowledge" as two key behavioral domains commonly linked to noncompliance. This suggests that hand hygiene interventions should target both "conscious decision making and automatic processes (working on “auto-pilot”) by, for example, using “If-Then” plans and ensuring good knowledge.” Fuller *et al.* argued that a TDF to investigate HCW’s “real-time” explanations of noncompliance provides a "coherent" way to design hand hygiene interventions.[99]

In summary, understanding existing causes of poor hand hygiene compliance and which barriers and enablers need to be addressed is an important requirement for designing hand hygiene promotion interventions having a good chance of success.

Implementing the intervention

Huis *et al.* published a systematic review of hand hygiene improvement strategies and applied a behavioural approach in their analysis.[100] This led to a taxonomy of behavioural change techniques which was used to identify targeted determinants. Determinants of behaviour change are the determinants targeted by a systematically developed strategy i.e. things that have been identified for altering behaviours. Theoretically, the application of a chosen behaviour change activity as part of the hand hygiene improvement strategy will alter a specific behavioural determinant, which in turn will change behaviours. An example application of behaviour change techniques for improving hand hygiene from this study is presented in Table 2.7.

Table 2.5: Steps for developing a theory-informed implementing intervention, from French *et al.,* 2012[94]

Step	**Tasks**
STEP 1: Who needs to do what, differently?	• Identify the evidence-practice gap • Specify the behaviour change needed to reduce the evidence-practice gap • Specify the health professional group whose behaviour needs changing
STEP 2: Using a theoretical framework, which barriers and enablers need to be addressed?	• From the literature, and experience of the development team, select which theory (ies), or theoretical framework(s), are likely to inform the pathways of change • Use the chosen theory(ies), or framework, to identify the pathway(s) of change and the possible barriers and enablers to that pathway • Use qualitative and/or quantitative methods to identify barriers and enablers to behaviour change
STEP 3: Which intervention components (behaviour change techniques and mode(s) of delivery) could overcome the modifiable barriers and enhance the enablers?	• Use the chosen theory, or framework, to identify potential behaviour change techniques to overcome the barriers and enhance the enablers • Identify evidence to inform the selection of potential behaviour change techniques and modes of delivery • Identify what is likely to be feasible, locally relevant, and acceptable and combine identified components into an acceptable intervention that can be delivered
STEP 4: How can behaviour change be measured and understood?	• Identify mediators of change to investigate the proposed pathways of change • Select appropriate outcome measures • Determine feasibility of outcomes to be measured

Forty-one studies of experimental and quasi-experimental research on hand hygiene improvement strategies were reviewed in this study. The most frequently addressed determinants were knowledge, awareness, action control, and facilitation of behaviour. Relatively few studies addressed social influence, self-efficacy, attitude, and intention. There were thirteen studies using controlled designs to assess the effects of improvement strategies on hand hygiene behaviour. The reported effectiveness of the strategies varied substantially, but most controlled studies showed positive results as assessed by relative difference in hand hygiene compliance. Relative difference is defined here as the compliance in the intervention group minus the compliance from the control group) divided by the compliance from the control group after the intervention. The median effect for these strategies was a relative difference (improvement) of 17.6% in hand hygiene compliance. The effect size from one controlled study addressing two determinants was a relative difference of 25.7%. The relative difference increased from 42.3% in the three studies addressing three determinants to 43.9% for the two studies addressing four determinants. The relative difference was 49.5% for the three studies that addressed five determinants. By focusing on determinants of behaviour change, the authors argued, it is possible to find valuable and otherwise hidden components in hand hygiene improvement strategies. The authors also argued that addressing only determinants such as knowledge, awareness, action control, and facilitation is not enough to change hand hygiene behaviour. Addressing combinations of different determinants showed better results. This indicated a need for more creativity in the application of alternative improvement activities addressing determinants such as social influence, attitude, self-efficacy, or intention.

In a study by McAteer *et al.*, semi-structured interviews to identify the barriers to and facilitators of implementation were performed with 17 ward coordinators who had delivered a feedback intervention to improve hand hygiene.[101] The lower scoring domains and those indicating low likelihood of successful implementation of trial interventions were “environmental context and resources”, “beliefs about capabilities”, “social influences”, and “emotion”. The lowest scoring domain was “environmental context and resources”. Lack of time, understaffing, perceived negativity from co-workers, and stress were identified as challenges. Ward coordinators described difficulties finding time to implement the trial within the context of existing routines and increased clinical workload because of staffing issues. In these instances, implementing the trial became a low priority. Ward coordinators stated that, whereas they felt equipped to deliver the intervention, they had concerns about their capabilities to do so within the context of available time and staffing. The higher scoring domains and those indicating greater likelihood of successful implementation of the trial were “behavioral regulation, “motivation”, “skills, “knowledge”, and “professional role”. Ward coordinators reported that they believed they had the relevant skills, understanding, and motivation to implement the intervention.[101]

In summary, behaviour change theory and techniques can help find new pathways for increasing hand hygiene and can also be valuable for classifying and understanding previously described approaches.

Table 2.6: Example of application of behaviour change techniques for improving hand hygiene behaviour by determinants from a systematic review of studies of the promotion of hand hygiene in HCWs, from Huis *et al.*, 2012[100]

Determinants	Behaviour change technique	Description of the activity in studies
Knowledge	Provide general information	Educational sessions or educational materials
	Increase memory or understanding of information	Group discussion, answering questions, clarification
Awareness	Risk communication	Information about risks of non-adherence or inadequate hand hygiene (infection rates, costs)
	Delayed feedback of behaviour	Overview of recorded hand hygiene behaviour
	Direct feedback of behaviour	Using a system to make professionals aware of their hand hygiene behaviour soon after planned execution
Social influence	Provide information about peer behaviour	Information about peers' opinions of correct hand hygiene
	Provide opportunities for social comparison	Group sessions with peers in which discussion and social comparison of hand hygiene practices can occur
	Mobilise social norm	Exposing the professional to the social norm of important others (not peers) such as opinion leaders
Attitude	Persuasive communication	Positive consequences of proper hand hygiene
	Reinforcement of behavioural progress	Praise, encouragement, or material rewards

Table 2.6: Example of application of behaviour change techniques for improving hand hygiene behaviour by determinants from a systematic review of studies of the promotion of hand hygiene in HCWs, from Huis *et al.*, 2012[100] (cont.)

Determinants	Behaviour change technique	Description of the activity in studies
Self-efficacy	Modeling	Use of a role model. Demonstration of proper hand hygiene behaviour in group, class, or team
	Verbal persuasion	Messages designed to strengthen control beliefs about the way of performing correct hand hygiene
	Guided practice	Teaching skills and providing feedback. Specific instruction for correct hand hygiene behaviour
	Plan coping responses	Identification and coping with potential barriers
	Set graded tasks, goal setting	Desired hand hygiene behaviour is achieved with a stepwise model
Intention	General intention information	Explanation of the goals and targets concerning hand hygiene
	Agree to behavioural contract	Contract or commitment with formulated goals of hand hygiene behaviour
Action control	Use of cues	Reminders
Facilitation of behaviour	Provide materials to facilitate behaviour	Supportive materials are provided for the healthcare workers
	Continuous professional support	Involves service provided by infection control team or working group, and/or an additional nurse who attends the implementation

2.5 Interventions to improve hand hygiene with recommendations of the World Health Organization

2.5.1 The multimodal strategy

The WHO report on implementing their multimodal improvement strategy argued equal importance should be attached to each component and that each component requires efforts to achieve effective implementation and maintenance, though hospitals around the world may have progressed to different levels in each of these strategies.[46] A multimodal strategy has been found to be an effective way to improve compliance in HCWs, based on an analysis of evidence from higher quality studies in a recent systematic review and network meta-analysis.[82]

The components of the multimodal strategy, as described by the WHO in their guide to implementation,[46] are:

1. *System change: ensuring that the necessary infrastructure is in place to allow health-care workers to practice hand hygiene. This includes two essential elements:*
    - *access to a safe, continuous water supply as well as to soap and towels;*
    - *readily accessible alcohol-based handrub at the point of care.*
2. *Training / Education: providing regular training on the importance of hand hygiene, based on the "My 5 Moments for Hand Hygiene" approach, and the correct procedures for handrubbing and handwashing, to all health-care workers.*
3. *Evaluation and feedback: monitoring hand hygiene practices and infrastructure, along with related perceptions and knowledge among health-care workers, while providing performance and results feedback to staff.*

4. *Reminders in the workplace: prompting and reminding health-care workers about the importance of hand hygiene and about the appropriate indications and procedures for performing it.*
5. *Institutional safety climate: creating an environment and the perceptions that facilitate awareness-raising about patient safety issues while guaranteeing consideration of hand hygiene improvement as a high priority at all levels, including*
    - *active participation at both the institutional and individual levels;*
    - *awareness of individual and institutional capacity to change and improve (self-efficacy); and*
    - *partnership with patients and patient organizations*

2.5.2 My five moments

Within the framework of the WHO's First Global Patient Safety Challenge known as "Clean Care is Safer Care,"[47] an evidence-based, user-centered concept, "My five moments for hand hygiene,"(Table 2.8) was developed for measuring , teaching, and reporting hand hygiene behaviour. This concept is an essential part of the WHO's hand hygiene improvement strategy which aims to translate the WHO Guidelines on Hand Hygiene in Health Care into practice.[89]

Table 2.7: The "My five moments for hand hygiene" concept and transmission risks, from Sax *et al.,* 2009[102]

Indication term for hand hygiene	**Departure hand-to surface exposure**	**Hand transition and microorganism transmission risk**	**Arrival hand-to-surface exposure**	**Major targeted negative infectious outcome**	**Examples**
Before touching a patient	Surface outside the patient zone	Hand transmission of microorganisms from the health care environment to the patient	Patient's intact skin and other surfaces inside the patient zone	Colonization of the patient by hospital pathogens	Touching the door handle and then shaking hands with the patient
Before aseptic/ clean procedure	Any surface	Hand transmission of microorganisms from any surface (including the patient skin) to a site that would facilitate invasion and infection	Critical site for infection in the patient	Endogenous or exogenous infection of the patient	Preparing the material and then giving an injection
After body fluid exposure risk	Critical site for body fluid exposure in HCWs	Hand exposure to patient's body fluids potentially containing blood-borne or other pathogens	Any surface	Infection of the HCW by patient bloodborne pathogens	Drawing blood and then adjusting the infusion drop count

Table 2.7: The "My five moments for hand hygiene" concept and transmission risks, from Sax *et al.,* 2009[102] (cont.)

Indication term for hand hygiene	Departure hand-to surface exposure	Hand transition and microorganism transmission risk	Arrival hand-to-surface exposure	Major targeted negative infectious outcome	Examples
After touching a patient	Patient's intact skin and other surfaces inside the patient zone	Hand transmission of microorganisms from the patient flora to other surfaces in the health care setting	Surface outside the patient zone	Dissemination of patient flora to the rest of the health care environment and infection of HCWs	Shaking hands with the patient, arranging the bedside table, and then touching the door handle
After touching patient surroundings (without touching the patient during the same care sequence)	Surface inside the patient zone if the patient was not touched	Hand transmission of microorganisms from the patient flora to other surfaces in the health care setting	Surface outside the patient zone	Dissemination of patient flora to the rest of the health care environment and colonization of HCWs	Touching the bed rail (without touching the patient) and then touching the door handle

2.5.3 Applying the WHO strategy in healthcare settings

A systematic review of methodologically strong studies to assess the relative effectiveness of the WHO Five Multimodal Hand Hygiene Improvement Strategy (WHO-5) and other strategies for improving compliance with hand hygiene in healthcare workers in hospital settings during 1980 to 2014 was recently published by Luangasanatip *et al.*[82] This review also aimed to summarize associated information on use of resources.

Forty-one studies met the inclusion criteria, including 6 randomised controlled trials, 32 interrupted time series studies, one non-randomized trial, and two controlled before-after studies.

Key findings from this review are:

i. Network meta-analyses of included studies provided evidence that the WHO campaign is effective at increasing compliance with hand hygiene in healthcare workers.
ii. There was evidence that additional interventions (used in conjunction with the WHO campaign elements), including goal setting, reward incentives, and accountability, can lead to further improvements.
iii. Reporting on resource implications of such interventions is limited.

Nineteen studies reported clinical outcomes. These outcome data were consistent with clinically important reductions in rates of infection resulting from improved hand hygiene for some but not all important hospital pathogens.

Network meta-analysis indicated considerable uncertainty in the relative effectiveness of interventions, but nonetheless provided evidence that WHO-5 is effective and that compliance can be further improved by adding interventions including goal setting, reward incentives, and accountability (Figure 2.2).

Table 2.8: Description of hand hygiene intervention by components, from Luangasanatip *et al.,* 2015. [82]

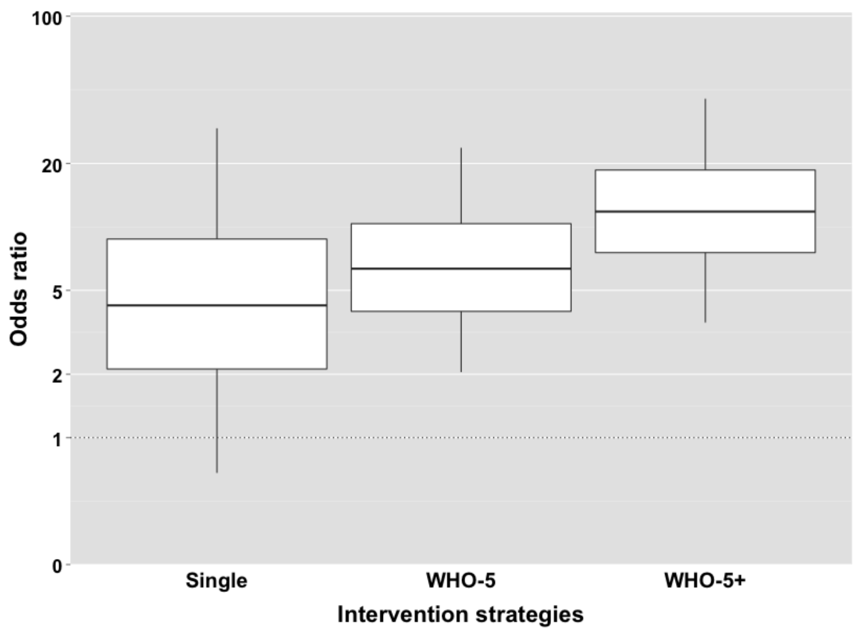
Type of Hand hygiene intervention component	Description
1. System change [a]	Ensuring necessary infrastructure is available including a) access to water, soap and towels and b) alcohol-based handrub at the point of care.
2. Education and Training	Providing training or educational programme on the importance of hand hygiene and the correct procedures for hand hygiene, for healthcare workers.
3. Feedback	Monitoring hand hygiene practices among healthcare workers while providing the compliance feedback to staff.
4. Reminders at workplace	Prompting healthcare workers either through printed material, verbal reminders, electronic communications or other methods, to remind them about the importance of hand hygiene and the appropriate indications and procedures.
5. Institutional safety climate	Active participation at institutional level, creating an environment allowing prioritization of hand hygiene.
6. Goal-setting	Setting of specific goals aimed at improving hand hygiene compliance, which may both apply at the individual and group level and may include healthcare associated infection rates.
7. Reward incentives	Interventions involved with providing any reward incentive for the participants once they achieve a particular task or reach a certain level of hand hygiene compliance. Both non-financial and financial rewards are included.
8. Accountability	Interventions involved with improving healthcare workers' accountability both at an individual and unit level.

[a] if the intervention period included changing the place or formulation or installing more dispensers of alcohol based handrub, the baseline intervention was counted as no intervention or standard practice (no system change component) although the alcohol-based handrub had been used during the baseline.

This systematic review also highlighted methodological weaknesses in many hand hygiene studies and noted that few studies meeting minimal quality criteria came from developing countries. A similar finding came from the systematic review of Gould *et al.* in 2010, though only four studies met the inclusion criteria in this review.[103]

In summary, there is good evidence that the WHO-5 intervention is effective at promoting hand hygiene. Stronger study designs including randomized controlled trials and interrupted time series analyses should be more frequently used in the evaluation of interventions to promote hand hygiene.

Figure 2.2: Box-and-whiskers plot showing relative efficacy of different hand hygiene intervention strategies compared with standard of care estimated by network meta-analysis from interrupted time series studies. Lower and upper edges represent 25th and 75th percentiles from the posterior distribution; the central line represents the median. Whiskers extend to the 5th and 95th percentiles. Intervention strategies were single intervention; WHO-5; and WHO-5+ (WHO-5 with incentives, goal-setting, or accountability), from Luangasanatip *et al.,* 2015.[82]



2.6 The stepped wedge cluster randomized trial

This section is concerned with the study design to be used to evaluate the hand hygiene intervention as described in Chapter 5. It considers: i) what is the stepped wedge cluster randomized trial?, ii) study rationale , and iii) the stepped wedge cluster randomized trial use in health behaviour interventions.

2.6.1 What is the stepped wedge cluster randomized trial?

The randomized controlled trial (RCT) is generally considered the 'gold standard' for evaluating the effectiveness of an intervention. But the standard RCT will not be appropriate or practical for some interventions, for example health education programmes where the intervention is applied to a group of participants. Stepped wedge cluster randomized controlled trials (SW-RCTs) may be more appropriate in such cases. A stepped wedge design is a type of cluster randomized controlled trial which is appropriate when there are prior reasons to believe the intervention will be beneficial (as opposed to equipoise) and when it is impractical to deliver the intervention to all study units simultaneously.[104] The SW-RCT is increasingly being used to evaluate "service delivery" type interventions.[105]

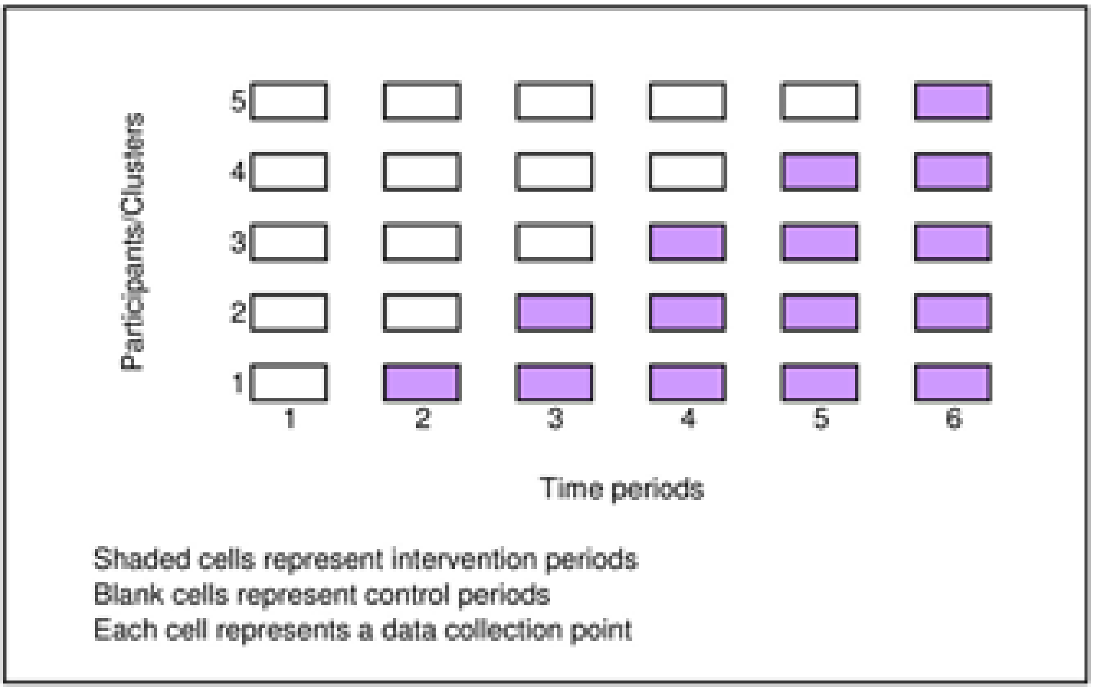
2.6.2 Study rationale

This SW-RCT design is useful when i) there is prior belief that the intervention will do more good than harm, ii) there are logistical, practical or financial constraints to applying the intervention simultaneously to multiple groups, and iii) there is a need to evaluate a public policy intervention that is being rolled-out prior to effectiveness being established.[106]

In a stepped wedge design, an intervention is rolled-out sequentially to the trial participants (sometimes individuals, but more typically clusters of individuals) over a number of time periods. The order in which these clusters get the intervention is determined at random according a specified schedule. By the end of the random allocation the intervention will have been delivered to all individuals or groups. Stepped wedge designs incorporate data collection at each time point for each group, both before and after the intervention are delivered.

An example of the logistics of a stepped wedge trial design is shown in Figure 2.3, which shows a stepped wedge design with five steps. Data analysis to determine the overall effectiveness of the intervention subsequently involves comparison of the data points in the control section of the wedge with those in the intervention section.[106]

Figure 2.3: Example of a stepped wedge design ,from Brown and Lilford, 2006[106]



2.6.3 The stepped wedge cluster randomized trial in health behaviour research

The SW-RCT design in increasingly used to assess health behaviour interventions in many studies involving health behaviour (including hand hygiene behaviour), as highlighted in two systematic reviews.[106, 107]

To take one example, the Feedback Intervention Trial (FIT) was a 3-year SW-RCT of 36 months duration aimed at improving hand-hygiene compliance in UK healthcare workers.[108] The study compared routine practice with a feedback intervention developed within a behavioural theoretical framework. The intervention was rolled out sequentially in 16 English/Welsh Hospitals (clustering within clustering) switching from control to intervention every 2 month at 5 different time points after an initial baseline period. All study wards within the hospital were allocated to start the intervention concurrently. The primary outcome was hand hygiene compliance. The study found significant sustained improvements in hand hygiene compliance in wards implementing the intervention. However, not all wards implemented the intervention according to protocol and the difficulties in implementation, and lacks of fidelity to intervention were found to be important issues in this study.

In summary, the SW-RCT is a good study design for evaluating the effectiveness of hand hygiene interventions, because all HCWs should receive this intervention.

Summary

Improving hand hygiene compliance amongst HCWs is one of the simplest and most effective measures for preventing HCAIs. However, only a few studies have evaluated the effectiveness of interventions for improving hand hygiene compliance using strong study designs, and almost all of these have been in high income countries. The development and evaluation of intervention to reduce HCAI in resourced-limited hospital settings is needed.

Chapter 3

Burden of hospital-acquired and healthcare-associated infections in a resource-limited hospital setting

3.1 Introduction

Nosocomial infection is a major cause of morbidity and mortality in those who receive medical care or treatment in a hospital or hospital-like setting, and surveillance must be regularly performed in a systematic way in order to reduce the rates of the infection.[109] However there is a paucity of information about their epidemiology from developing countries despite the fact that such countries are believed to have the highest burden of nosocomial infection and account for most of the world's population.[3] This is particularly true for nosocomial bacteraemias which are frequently used as indicators of trends in overall nosocomial infection in developed countries because of the availability of clear definitions and clinical relevance.[109, 110]

A recent comprehensive systematic review found only 13 studies of healthcare-associated bloodstream infection from developing countries between 1995 and 2008, with only six studies in the Southeast Asia region and none from the Western Pacific region.[3] For example, the reported incidence rates of hospital-acquired bacteraemia (HAB) through active surveillance were 1.0 per 1,000 patient-days in a district hospital in Kenya between 2002 and 2009[111], and 1.2 per 1,000 patient-days in a university hospital in Iran in 2006.[112] This lack of information is a consequence, at least in part, of the paucity of reliable surveillance systems for such outcomes in resource-limited settings.

Moreover, published literature from developing countries is often from better resourced or university hospitals [111, 112] and may not provide a reliable basis for generalization to public hospitals in those countries.

In this study, multiple sources of routine surveillance data are combined including microbiology databases, hospital admission databases and the national death registry from a sample of provincial hospitals in northeast Thailand.[113] The objectives were to demonstrate trends in incidence, antibiotic-resistance and mortality associated with HAB and healthcare-associated bacteraemia (HCAB) over a seven year period.

3.2 Materials and Methods

3.2.1 Study population

Northeast Thailand consists of 20 provinces, covers 170,226 km^2 and had an estimated population in 2010 of 21.4 million. Each province has a provincial hospital that provides care to people living within its catchment area and acts as a referral hospital for smaller district hospitals. The number of beds per provincial hospital ranges from 200 to 1000, and all provincial hospitals are equipped with intensive care units (ICUs). Severely ill patients presenting to district hospitals are often referred to provincial hospitals. Provincial hospitals are equipped with a microbiology laboratory that provides a bacterial culture service, while district hospitals normally do not have such facilities. All microbiology laboratories in provincial hospitals use standard methodologies for bacterial identification and susceptibility testing provided by the Bureau of Laboratory Quality and Standards, Ministry of Public Health, Thailand.[114]

3.2.2 Study design

A retrospective study was conducted, using surveillance data from all provincial hospitals in northeast Thailand. The data were collected as previously described.[110] In brief, the director of each hospital was contacted and given information on the study. For those hospitals that agreed to participate, data were collected from the microbiology and hospital databases between Jan 2004 to Dec 2010. Admission number (AN) was used as the record linkage between the two databases, and hospital number (HN) was used to identify individuals who had repeated admissions. The death registry for northeast Thailand between Jan 2004 to Jan 2011 was obtained from the Ministry of Interior, Thailand, and used to identify patients who were discharged from hospital and died within 30 days after discharge from the hospital.

3.2.3 Ethical review and study permissions

Ethical permission for this study was obtained from the Ethical and Scientific Review Committees of the Ministry of Public Health, Thailand, and of Faculty of Tropical Medicine, Mahidol University (Appendix B.1). Written consent was given by the director of the hospitals to use the routine hospital database for research. Consent was not sought from the patients as this was a retrospective study, and the Ethical and Scientific Review Committees approved the process.

3.2.4 Data collection

The microbiology laboratory data collected were HN, AN, specimen type, specimen date, culture result, and antibiotic susceptibility profile (antibiogram). Hospital data were collected from the routine in-patient discharge report (Report 501), which is regularly completed by attending physicians and reported to the Ministry of Public Health, Thailand, as part of national morbidity and mortality reporting system. The data collected were HN, AN, national identification 13-digit number, gender, age, admission date, discharge date, and outcome. A single outcome variable is required by this reporting system, which is completed by the attending physicians and categorized as cured, improved, not improved, transfer to another hospital, refusal of treatment, or died. Date of death was also extracted from this record. Data collected from the death registry obtained from the Ministry of Interior were national identification 13-digit number and date of death. Data are not suitable for public deposition due to ethical restrictions. Raw database requests may be made to the director of each participating hospital (Appendix B.2).

3.2.5 Definitions

Bacteraemia was classified as community-acquired bacteraemia (CAB), HAB or HCAB. CAB was defined as the isolation of a pathogenic organism from blood taken in the first 2 days of admission and without a hospital stay in the 30 days prior to admission.[110] HAB was defined as the isolation of a pathogenic organism from blood taken after the first 2 days of admission.[59, 115] HCAB was defined as the isolation of a pathogenic organism from blood taken in the first 2 days of admission and with a hospital stay within 30 days prior to the admission. Patients at risk of HCAB were those with a hospital stay within 30 days prior to the admission. Patients were considered at risk of HAB after they stayed in the hospital for more than 2 days.

Because of the difficulty in establishing their clinical significance, organisms frequently associated with contamination including coagulase-negative *staphylococci*, Viridans group *streptococci*, *Corynebacterium* spp., *Bacillus* spp., *Diptheroid* spp., *Micrococcus* spp., and *Propionibacterium* spp. were excluded from the analysis.[116] Organisms that produced an extended-spectrum β lactamase (ESBL) were defined using standard methodologies for bacterial identification and susceptibility testing provided by the Bureau of Laboratory Quality and Standards, Ministry of Public Health, Thailand.[114] All patients with bacteraemia caused by *B. pseudomallei* were categorized as CAB because this organism is not a cause of HAB or HCAB.[117] Polymicrobial infection was defined in patients who had more than one species of pathogenic organisms isolated from the blood during the same episode. Information on patients with a first CAB episode has been published previously.[110] In this study, patients with a first episode of HAB or HCAB were evaluated in relation to epidemiology and mortality.

The 30-day mortality of HAB was determined on the basis of a record of death within 30 days of the positive blood culture taken as recorded in the routine hospital database or by a record of death in the national death registry. The 30-day mortality of HCAB was defined as death within 30 days of the admission date. The incidence rate of HAB was calculated as the number of HAB per 1,000 patient-days at risk. The cumulative incidence of HCAB was calculated as the number of HCAB per 100 readmissions. To avoid the assessment of multiple outcomes for a single patient, in the event that a patient had more than one episode of bacteraemia (either HAB and/or HCAB) only the first episode was included in the study.

3.2.6 Statistical analysis

All analyses were performed using STATA version 12.0 (StataCorp LP, College station, Texas). Poisson regression models were used to calculate incidence rate ratios, and logistic regression models were used to calculate odds ratios. Fisher's exact test was used to compare categorical variables. The Mann-Whitney test was used to compare continuous variables. A non-parametric test for trend was used to assess change in proportion over time and stratified by hospital (using the *npt_s* command in STATA).

3.3 Results

All 20 provincial hospitals in northeast Thailand were contacted to participate in this study. Agreement was obtained from 15 (75%) hospitals, of which 10 had microbiological laboratory and hospital databases as electronic files in a readily accessible format (Appendix B.3). Of the 10 hospitals included in the analysis, 3 (30%) had data available for the period 2004–2010, 1 (10%) between 2006–2010, 2 (20%) between 2007–2010, 3 (30%) between 2008 and 2010, and 1 (10%) between 2009–2010 (Table 3.1 and Table 3.2). The median bed number was 450 beds (range 300 to 1,000 beds). A total of 1,969,474 admission records from 1,372,446 patients were evaluated, of which 21,438 (1.1%) admission records had at least one blood culture positive for pathogenic organisms during admission. A total of 3,451 (16.1%) episodes were defined as hospital-acquired bacteraemia (HAB), 2,302 (10.7%) episodes were healthcare-associated bacteraemia (HCAB) and 15,685 (73.2%) episodes were community-acquired bacteraemia (CAB). Multiple episodes of HAB and HCAB were noted in 26 and 102 patients, respectively. Only the first episodes of HAB and HCAB in 3,424 and 2,184 patients, respectively, were included in further analysis.

3.3.1 Incidence of HAB and HCAB

The average incidence rate for HAB during the 7-year study period was 0.7 per 1,000 patient-days, with an overall increase in rate over time. The incidence rate of HAB increased from 0.6 in 2004 to 0.8 per 1,000 patient-days in 2010 ($p<0.001$) (Table 3.1).

Table 3.1: Incidence rate of hospital-acquired bacteremia (HAB) and associated death rate between 2004 and 2010 in northeast Thailand

Year	Total number of hospitals with available data	Total number of hospital admission	Total number of hospital admissions at risk of HAB*	Total number of patients with HAB	Deaths associated with HAB	30-day mortality associated with HAB	Incidence rate for HAB (per 1,000 patient-days)
2004	3	129,376	74,272	212	90	42.5%	0.6
2005	3	138,816	79,254	292	120	41.1%	0.8
2006	4	187,812	102,948	259	100	38.6%	0.5
2007	6	241,208	129,574	366	185	50.5%	0.6
2008	9	372,564	199,154	640	281	43.9%	0.7
2009	10	453,791	239,814	840	388	46.2%	0.8
2010	10	445,907	244,427	815	395	48.5%	0.8
Overall	**10**	**1,969,474**	**1,069,443**	**3,424**	**1,559**	**45.5%**	**0.7**

* Patients at risk of HAB were patients who stayed in the hospital longer than 2 days.

Of 1,969,474 admission records, 119,286 (10.1%) had a hospital stay within 30 days prior to admission and were at risk of HCAB. The cumulative incidence for HCAB during the 7-year study period was 1.8 per 100 readmissions, with an overall increase in the cumulative incidence over time. The cumulative incidence of HCAB increased from 1.2 in 2004 to 2.0 per 100 readmissions in 2010 (p<0.001) (Table 3.2). The incidence rate of HAB and HCAB varied by hospitals (Appendix B.4), but the overall increasing trends were observed in most hospitals.

3.3.2 Demographic risk factors for HAB and HCAB

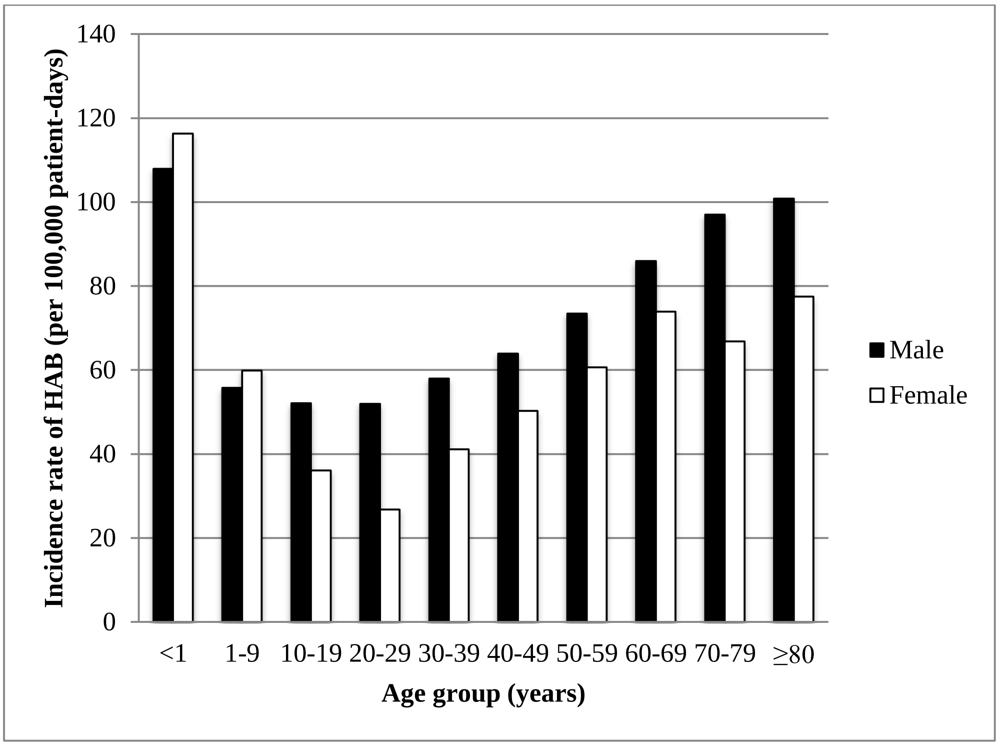
Of 3,424 patients with a primary episode of HAB, 2,000 (58.4%) were male and 1,424 (41.6%) were female. The median age was 51 years (interquartile range [IQR] 16–67 years, range 0–88 years). The median time from hospital admission to bacteraemia was 8 days (IQR 4–15 days, range 3–105 days). The median length of stay for patients with HAB was longer than patients who were at risk of, but did not develop HAB (18 vs. 4 days, p<0.001). The overall incidence rate of HAB was higher in males than in females (0.8 vs. 0.6 per 1,000 patient-days, incidence rate ratio [IRR] 1.21; 95% confidence interval [CI] 1.13 to 1.30, p<0.001) (Figure 3.1). The incidence rates of HAB were highest in infants (1.1 per 1,000 patient-days), and in those older than 80 years of age (0.9 per 1,000 patient-days).

Table 3.2: Cumulative incidence of healthcare-associated bacteremia (HCAB) and associated death rate between 2004 and 2010 in northeast Thailand

Year	Total number of hospitals with available data	Total number of hospital admission	Total number of hospital admission at risk of HCAB*	Total number of patients with HCAB	Deaths associated with HCAB	30-day mortality associated with HCAB	Cumulative incidence for HCAB (per 100 readmissions)
2004	3	129,376	7,259	86	44	51.2%	1.2
2005	3	138,816	8,266	125	41	32.8%	1.5
2006	4	187,812	10,960	157	68	43.3%	1.4
2007	6	241,209	14,234	272	117	43.0%	1.9
2008	9	372,564	22,601	435	198	45.5%	1.9
2009	10	453,790	26,969	527	206	39.1%	2.0
2010	10	445,907	28,997	582	239	41.1%	2.0
Overall	**10**	**1,969,474**	**119,286**	**2,184**	**913**	**41.8%**	**1.8**

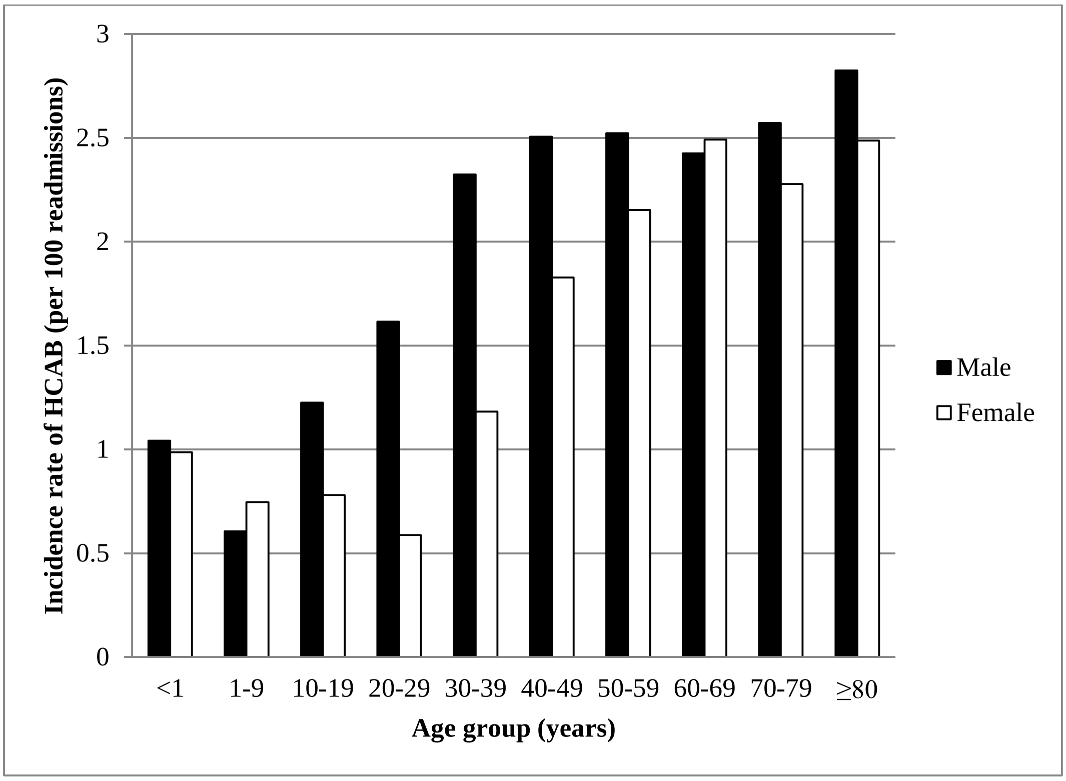
* Patients at risk of HCAB were patients who had a hospital stay within 30 days prior to the admission.

Figure 3.1: Age- and gender- specific incidence rate of hospital-acquired bacteraemia (HAB) between 2004 and 2010 in northeast Thailand



Of 2,184 patients with a primary episode of HCAB, 1,166 (53.4%) were male and 1,018 (46.6%) were female. Median age was 57 years (IQR 41–70 years, range 0–89 years). The median time between prior and study admission was 11 days (IQR 6–19 days, range 1–30 days). The median length of stay for patients with HCAB was longer than patients who were at risk of, but did not present with HCAB (6 vs. 3 days, $p<0.001$). Male gender was associated with a higher risk of HCAB (odds ratio [OR] 1.29; 95%CI 1.18 to 1.40, $p<0.001$) (Figure 3.2). The incidence rates of HCAB were high in infants (1.1 per 100 readmission), and very high in those older than 30 years of age (Figure 3.2).

Figure 3.2: Age- and gender- specific incidence rate of healthcare-associated bacteraemia (HCAB) between 2004 and 2010 in northeast Thailand



3.3.3 Pathogenic organisms associated with HAB and HCAB

Of all pathogenic organisms causing HAB, 2,313 (67.6%) were Gram-negative bacteria, 885 (25.8%) were Gram-positive bacteria, 81 (2.4%) were fungi, 3 (0.1%) were *Mycobacterium* spp., and 141 (4.1%) were polymicrobial (Table 3.3). The most common pathogens identified were *Acinetobacter* spp. (16.2%), *Klebsiella pneumoniae* (13.9%), *Staphylococcus aureus* (13.9%), *Escherichia coli* (12.6%), and *Pseudomonas* spp. (10.5%). Amongst *S. aureus* HABs, the proportion of meticillin-resistant *S. aureus* (MRSA) was 37.0% (176/476). Corresponding proportions of extended-spectrum β lactamase (ESBL)-producing *E. coli* and *K. pneumoniae* were 38.9% (169/434) and 59.3% (283/477), respectively.

Table 3.3: Pathogenic organisms isolated from 3,424 patients with primary episode of hospital-acquired bacteraemia (HAB) and 2,184 patients with primary episode of healthcare-acquired bateraemia (HCAB) in northeast Thailand between 2004 and 2010

Organisms	HAB	HCAB
Gram negative bacteria	**2,313 (67.6%)**	**1,470 (67.3%)**
Acinetobacter spp.	554 (16.2%)	124 (5.7%)
Escherichia coli		
ESBL –ve	265 (7.7%)	400 (18.3%)
ESBL +ve	169 (4.9%)	175 (8.0%)
Klebsiella pneumoniae		
ESBL –ve	194 (5.7%)	141 (6.5%)
ESBL +ve	283 (8.3%)	70 (3.2%)
Klebsiella spp.	122 (3.6%)	55 (2.5%)
Enterobacter spp.	155 (4.5%)	44 (2.0%)
Pseudomonas spp.	358 (10.5%)	205 (9.4%)
Other Gram negative	213 (6.2%)	256 (11.7%)
Gram positive	**885 (25.8%)**	**592 (27.1%)**
Stahpylococcus aureus		
Meticillin-susceptible	312 (9.1%)	238 (10.9%)
Meticillin-resistant	164 (4.8%)	67 (3.1%)
Enterococcus spp.	173 (5.1%)	74 (3.4%)
Other Gram positives	236 (6.9%)	213 (9.8%)
Fungi	**81 (2.4%)**	**24 (1.1%)**
Cryptococcus spp.	16 (0.5%)	20 (0.9%)
Candida spp.	59 (1.7%)	4 (0.2%)
Penicillium spp.	6 (0.2%)	-
Histoplasma spp.	1 (0.0%)	-
Mycobacterium spp.	3 (0.1%)	4 (0.2%)
Polymicrobial infections	141 (4.1%)	94 (4.3%)
Overall	**3,424 (100.0%)**	**2,184 (100.0%)**

Of all pathogenic organisms causing HCAB, 1,470 (67.3%) were Gram-negative bacteria, 592 (27.1%) were Gram-positive bacteria, 24 (1.1%) were fungi, 4 (0.2%) were *Mycobacterium* spp., and 94 (4.3%) were polymicrobial (Table 4.3.3). The most common pathogens identified were *E. coli* (26.3%), *S. aureus* (14.0%), *K. pneumoniae* (9.7%), *Pseudomonas* spp. (9.4%) and *Acinetobacter* spp. (5.7%). The proportion of ESBL-producing *E. coli*, ESBL-producing *K. pneumoniae* and MRSA were 30.4% (175/575), 33.2% (70/211), and 24.3% (74/305), respectively.

There were no differences in the patterns of common pathogens identified among different provinces or over the study period (Appendix B.5 and Appendix B.6). However, there was an overall increase in the proportions of ESBL-producing *E. coli* over time. From 2004 to 2010, the proportion of ESBL-producing *E. coli* causing HAB rose from 33.3% (10/30) to 51.5% (51/99) ($p = 0.005$) (Appendix B.7 and Appendix B.8), and that causing HCAB rose from 20.8% (5/24) to 32.9% (48/146) ($p<0.001$) (Appendix B.8 and Appendix B.9). The rising trend of ESBL-producing *E. coli* was observed in most hospitals, while a clear overall trend in the proportions of ESBL-producing *K. pneumoniae* or MRSA was not observed (Appendix B.10 and Appendix B.11).

3.3.4 Mortality associated with HAB and HCAB

Death within 30-days of the positive blood culture taken was identified in 1,559 patients with HAB, giving an overall 30-day mortality of 45.5% (Table 3.1). Considering all patients who were admitted for more than 2 days, the 30-day mortality of those with HAB was higher than those without HAB (45.5% [1,559/3,424] vs. 5.5% [45,807/833,818], $p<0.001$). Death in HAB patients occurred rapidly, with 749 of 1,559 deaths (48.0%) occurring within two days of the bacteraemia, 89 (5.7%) on day 3, and 74 (4.8%) on day 4. Death in HAB patients occurred in hospital in 58.4% (911/1,559) of cases, the reminder occurring after hospital discharge. There was no change in the 30-day mortality associated with HAB over time ($p = 0.58$).

Death within 30 days of admission with an episode of HCAB was identified in 913 patients, giving an overall 30-day mortality of 41.8% (Table 3.2). Considering all patients who had a hospital stay within 30 days prior to the admission, the mortality of those with HCAB was significantly higher than those without HCAB (41.8% [913/2,184] vs. 13.0% [15,168/117,102], p<0.001). Death in HCAB patients also occurred rapidly, with 410 of 913 deaths (45.7%) occurring within the first two days of admission, 54 (6.0%) on day 3, and 46 (5.1%) on day 4. Death in HCAB patients occurred in hospital in 43.2% (394/913) of cases, the reminder occurring after hospital discharge. There was no change in the 30-day mortality associated with HCAB over time (p = 0.36).

3.4 Discussion

This study showed that nosocomial infection is an increasing and important problem in northeast Thailand. The total number of deaths associated with HAB and HCAB in 2010 in our study (n = 634) were much higher than the total number of reported deaths due to important notifiable diseases such as dengue hemorrhagic fever (n = 139), influenza (n = 126), and leptospirosis (n = 43) during the same period countrywide.[118] There was a 32.3% increase in the incidence rate of HAB and 66.8% in the cumulative incidence of HCAB between 2004 and 2010 in northeast Thailand. These estimates reinforce the need for improved surveillance and prevention of nosocomial infection in developing countries.

An incidence rate of HAB in the participating hospitals in 2010 of 0.8 per 1,000 patient-days is higher than recent estimates in high-income countries, including 0.7 per 1,000 patient-days in Canada between 2007 and 2010,[119] 0.6 per 1,000 patient-days in the USA in 2005,[120] and 0.6 per 1,000 patient-days in Estonia between 2004 and 2005.[121] The Thai data are consistent with a recent review showing that other parameters used to estimate the burden of nosocomial infection in developing countries, such as prevalence of healthcare associated infections and ICU-acquired infections, are substantially higher than in developed countries.[3] The recent surveillance study conducted by the International Nosocomial Infection Control Consortium (INICC) also found that rates of central line associated bloodstream infection (CLAB) were significantly higher in ICUs in developing countries (6.8 per 1,000 central line-days) versus those reported in US ICUs (2.0 per 1,000 central line-days).[122] Our HAB incidence rate is, however, lower than HAB rates reported through active surveillance in some developing countries, including 1.0 per 1,000 patient-days in Kenya between 2002 - 2009,[111] and 1.2 per 1,000 patient-days in Iran in 2006.[112] It is possible that active surveillance may improve the detection of HAB and nosocomial infection in our geographical region.

During the study period, *Acinetobacter* spp. was the most common pathogen associated with HAB, followed by *K. pneumoniae* and *S. aureus*. *Acinetobacter* spp. is increasingly recognized as an important cause of nosocomial infection,[123] and our study confirms the importance this species as a leading cause of nosocomial infection in developing tropical countries.[3, 111, 124] The proportion of MRSA causing HAB in our setting (37%) was higher than that reported from developed countries,[119, 121, 125] and is consistent with a previous review of developing countries. An increase in the proportion of ESBL-producing *E. coli* causing HAB in our study is alarming, and is consistent with our previous report of an increase in the proportion of ESBL-producing organisms causing CAB in the same setting.[113]

This study highlights an increasing incidence of HCAB in developing countries. We used the total number of patients with readmission as a denominator to estimate the cumulative incidence of HCAB rather than the total number of patients with bacteraemia.[59, 115, 126] Our estimates showed that healthcare-associated infection was an increasing cause of readmission. The high proportion of MRSA, ESBL-producing *E. coli* and ESBL-producing *K. pneumoniae* amongst organisms causing HCAB was relatively similar to that causing HAB. Much lower resistance levels were seen in organisms causing CAB.[113] This is consistent with previous reports of HCAB in developed countries.[8, 9, 19]

The observed increase in incidence of both HAB and HCAB could be due to a combination of an increase in the incidence of nosocomial infection associated with a rise in the number of at-risk patients (for example aging patients and those with invasive interventions), and an increase in detection of HAB and HCAB due to improved healthcare practice over time. There is evidence that the incidence rate of CLAB in developing countries can be substantially reduced using a multi-dimensional infection control approach including a bundle of interventions, education, outcome surveillance, process surveillance, feedback on CLAB rate and performance feedback.[127-133]

The overall 30-day mortality with HAB of 45.5% in our setting is much higher than that typically reported in high-income countries,[119, 121, 134] but lower than the reported in-hospital mortality of 53% from a rural district hospital in Kenya.[111] The overall 30-day mortality with HCAB of 41.8% in our setting is also much higher than typically seen in high-income countries.[59, 115, 126] In addition to patient-related factors, the higher mortality typically seen in developing countries may be related to the proportion of antimicrobial-resistant pathogens, empirical antibiotic regimens used, and sub-optimal severe sepsis management in resource-limited settings.[111, 135] It is also possible that practice in high-income countries can detect milder bacteraemia cases such as cases due to intravenous device that is then rapidly removed, while the practice in low-income countries may be less likely to achieve this. The high mortality observed in our study also reflects post-discharge ascertainment of patient outcomes using the national death registry. We found that in 47.2% of fatal cases of HAB or HCAB death occurred after hospital discharge. This reflects a preference amongst people in the study area to die at home. Further studies need to explore how to reduce the mortality of patients with HAB and HCAB in resource-limited areas.

A limitation of this study is that more complete clinical data were not available. As data on central line days were not available, the incidence rate of CLAB per 1,000 central line days could not be estimated and benchmarked against other prospective studies.[136-153] As data on process surveillance were not available, the reasons for the increased incidence of HAB could not be systematically assessed.[138, 147, 154, 155] Another potential limitation is that blood cultures may not have been performed for all patients with a likelihood of nosocomial infection, and this might lead to an underestimation in the incidence of HAB and HCAB among participating hospitals. In addition, data on hospitalisation in other hospitals not participating in the study (for example, a district hospital or a private hospital in the province) were not available, which could have resulted in an underestimation of the incidence of HAB and HCAB in our study. It is also possible that some patients with HAB and HCAB in our study may have had contaminated cultures and were incorrectly counted. However, the high mortality in patients with HAB and HCAB suggested that true infection was more likely than culture contamination. Although our data showed that, in general, patients with HAB and HCAB stayed in the hospital longer than those without, the analysis did not take account of the high mortality associated with HAB and HCAB. The length of stay would be further extended if death of patients with HAB and HCAB could be reduced. Additional costs and extra length of stay attributable to HAB and HCAB will be further evaluated using health economic models.[156, 157]

Although monitoring of nosocomial infection in developing countries is hampered by incomplete routine notification, our study has shown that careful evaluation of readily available routinely collected databases can provide valuable information on the incidence and trend of HAB and HCAB. The methodology used in our study could be applied to other geographical areas where microbiological facilities are available to provide a more comprehensive global picture of the importance of nosocomial infection as a cause of death.

3.5 Conclusions

This study demonstrates a high and increasing incidence of HAB and HCAB in northeast Thailand. Gram-negatives were the most common organisms, and about half of all bacteraemias were caused by multi-drug resistant organisms with increasing proportions of ESBL-producing isolates, and very high associated mortality. *Acinetobacter* spp. is currently the most common cause of HAB in Thailand.

In some cases, information on nosocomial infection in developing countries can be obtained by integrating readily available databases. Linking routine clinical and laboratory databases can lead to a better understanding of the burden of HAI and help infection-control practitioners better target their efforts to reduce the incidence of HAI and associated mortality. Nosocomial infection is an increasing problem in Thailand, and effective interventions to combat this problem are needed.

Chapter 4

Application of the theoretical domain framework for behaviour change to explore noncompliance in hand hygiene behaviour among hospital healthcare workers

4.1 Introduction

Hand hygiene is recognized as being amongst the simplest and most cost-effective measures to reduce healthcare-associated infections (HCAIs). Its effectiveness was first demonstrated in the studies of Semmelweis[158] in 1847 where it was shown that cleaning hands of hospital staff with a chlorinated solution led to large reductions in the mortality rate among mothers delivering at the General Hospital of Vienna. More recently, one of the most well-known examples of hand hygiene interventions comes from an observational studies at the University Hospital of Geneva, where reported reductions in HCAIs were associated with big improvements in hand hygiene compliance, which improved progressively from 48% in 1994, to 66% in 1997 by implementing a hospital-wide programme, with special emphasis on bed-side, alcohol-based hand disinfection.[18]

The World Health Organization (WHO) emphasizes the importance of preventing HCAIs by giving priority to the promotion of hand hygiene best practices in health-care settings.[89] This may be particularly important in low and middle income countries (LMICs) which have the highest burden of disease due to HCAIs,[3, 159, 160] but where well-resourced national hand hygiene campaigns have been lacking.[82]

Poor adherence to recommended hand hygiene measures during routine patient care among healthcare workers (HCWs) remains a major problem,[21, 161] and compliance as low as 4% has been reported.[161] Factors associated with poor hand hygiene compliance have been reported from many observational and intervention studies and include internal and external factors. Internal factors include sex, professional category/role, experience of HCWs, knowledge, belief, attitude, awareness, positive role models, and perception.[21, 89, 161-164] In contrast, external factors include hospital ward, time of day or week, type and intensity of patient care, type of task, moment for performing hand hygiene, workload, activities with high risk of cross-transmission, understaffing or overcrowding, and a high number of opportunities for hand hygiene per hour of patient care.[64] Almost all of these studies were in developed countries,[89] and few high quality studies come from LMICs.[50, 89]

The underlying reasons for low levels of hand hygiene compliance are poorly understood, and little is known about current knowledge and beliefs amongst HCWs in resource-limited settings about the benefits of hand hygiene and infection control activities or potential obstacles to improving infection control.

Factors in noncompliance for hand hygiene behaviour have recently been studied by applying behavioral theories.[89] Hand hygiene behaviour is influenced by both individual (intrapersonal factors) and institutional (interpersonal and community factors) factors.[21]

The theoretical domain framework (TDF) is a framework of behaviour theories, developed from a synthesis of theories of behaviour change[88] with the aim of systematically identifying psychological and organisational theory relevant to health practitioner clinical behaviour change.[42] Recently, a number of studies have used the TDF to explore the determinants of hand hygiene behaviour amongst HCWs.[98, 100] This behavioural approach has also been used to identify key determinants of successful hand hygiene improvement strategies in a systematic review.[100]

The *WHO Guidelines on Hand Hygiene in Health Care* have been developed with the ultimate objective of changing the behaviour of individual HCWs to optimize compliance with hand hygiene.[64] A systematic understanding of the drivers of hand hygiene behaviour is needed, particularly in developing countries where the HCAI problems are typically greatest but where there has been little research into hand hygiene behaviour.

Understanding existing causes of poor hand hygiene compliance and which barriers and enablers need to be addressed is an important requirement for designing a hand hygiene promotion intervention having a good chance of success.[64, 94, 95]

Limited data are available concerning factors associated with poor hand hygiene adherence and interventions to improve hand hygiene practices among HCWs in developing countries.[25, 85, 86, 165-168] Few studies in resource-limited settings have systematically explored the factors affecting hand hygiene compliance at both the individual and institutional levels. In this study, both barriers and enablers associated with hand hygiene behaviour are systematically explored. The aims are to identify the behavioural determinants –both barriers and enablers—that may affect hand hygiene behaviour of HCWs.

4.2 Methods

4.2.1 Study population

Participants were recruited from HCWs in all wards in a 1000-bed tertiary hospital in northeast Thailand. Only HCWs having direct contact with patients were included (including physicians, nurses, practical nurses, nurse-aids, medical students and student nurses).

Inclusion criteria

HCWs having direct contact with patients who worked in all intensive care units (ICUs) and all inpatient wards.

4.2.2 Study design

A cross-sectional study was conducted. Mixed methods including qualitative and quantitative approaches were employed to systematically explore the determinants of hand hygiene behaviour amongst HCWs. Qualitative methods were employed in focus group discussions and semi-structured interviews, while quantitative methods were employed in a self-administrated questionnaire and direct observation on hand hygiene practices.

Focus group discussions were used to identify interpersonal, institutional and community factors affecting hand hygiene behaviour in each HCW group. Semi-structured interviews were used to identify interpersonal, institutional and community factors including organizational factors. A self-administrated questionnaire was used to address knowledge and beliefs about hand hygiene in the entire population of hospital HCWs with patient contact. Direct observation was used to assess the current practice of hand hygiene behaviour from selected HCWs.

4.2.3 Ethical review and study permissions

The ethics committees of the hospital site and the Faculty of Tropical Medicine, Mahidol University approved the research protocol and all study forms (Appendix C.1). The director of the hospital site approved the research plan and gave permission to conduct the study.

4.2.4 Study procedure

The study procedure consisted of four sections: i) documentation preparation, ii) sampling and recruitment, iii) data collection, and iv) data analysis.

Documentation preparation

Documents were prepared for the focus group discussions, semi-structured interviews, self-administrated questionnaire, and direct observations. All documents were developed in the Thai language.

Preparing documents included the following steps:

1) Reviewing international guidelines for hospital hand hygiene and the literature on factors affecting hand hygiene compliance; reviewing the TDF definitions[88] on healthcare professional behaviours.[169]
2) Ensuring that questions on documents were based on applying TDF and the previously described barriers and enablers to hand hygiene practice based on previous reviews.
3) Working with the infection control team (ICT) of the hospital site to ensure that all questions were appropriate in this setting
4) Developing an observation form, to enable assessment of current hand hygiene practice in HCWs. This required working with the infection control team (ICT) at the hospital site to create a form which can be feasibly applied for the routine work of ICT as well as for the purpose of this study. Hand hygiene opportunities were defined according to the WHO Hand Hygiene Guidelines, [29] and classified as one of five moments for hand hygiene according to these guidelines.
5) Piloting the form amongst a sample of participants (n=30) working at the study site. Piloting indicated that providers clearly understood the form, and no changes were necessary.
6) Submitting all documents including the protocol, informed consent form, participant information sheet, form for hand hygiene observation and proposed questionnaire

(including a questionnaire for the focus group discussion, questionnaire for the semi-structured interviews, and the self-administrated questionnaire) to the relevant ethical committee.

Sampling and recruitment

i. A list of HCWs was provided by the hospital's Human Resources department. Recruitment documents (including an invitation letter, study information, an informed consent form, and a questionnaire) were sent to all eligible HCWs at all wards including 16 ICUs and 36 non-ICU in-patient wards. HCWs, who voluntarily agreed to participate in the study and signed the informed consent form, were included in the study. Participants who refused to participate in the study or refused to sign the informed consent form were excluded.

ii. For the self-administrated questionnaire, all participants who agreed to sign the informed consent form and complete the questionnaire were recruited.

iii. For focus groups, ten wards from four departments were purposively sampled to obtain a diverse range of participants in term of their professional role and clinical areas in which they worked. One representative of each type of HCW (including physicians, registered nurses (RNs), infection control ward nurses (ICWNs), and nurse-aides) joined in the focus group discussions.

iv. For semi-structured interviews, five selected key administrators, (including the director of the hospital, head of hospital infection control, head of laboratory, and attending physician), who were working in infection control at the hospital were invited to be participants.

v. Observations of hand hygiene practices were performed in the same wards as those used in focus groups discussion. Participants in observational activities were selected by choosing 6 HCWs of each job category including physicians, nurses, practical nurses, nurse-aides, medical students and student nurses working in that ward.

Data collection

i. The questionnaire survey was conducted during November 2010 to January 2011.

ii. The focus group discussion and semi-structured interviews were undertaken over a period of six months from April 2011. Focus group discussion and interviews were conducted in Thai and observed by members of the hospital ICT. Informed consent was obtained before starting each focus group and interview. HCWs that voluntarily agreed to participate in the study and signed the informed consent form were included in the study. Participants who refused to participate in the study or refused to sign the informed consent form were excluded. Participants were interviewed in their work place, in a private area which only the research team could access. Focus groups took place in a meeting room at the study site. Focus groups and interviews were noted on the form and recorded on audiotape.

iii. Observation of hand hygiene practices were performed in the same wards as those used in the focus groups discussion. Observations were performed by trained observers with a clear understanding of the WHO guidelines for hand hygiene.[102] Before collecting data, Cohen's kappa (for two raters) was used to assess inter-rater reliability.[170] Results from the observations were entered into an observation form derived from the WHO Hand Hygiene Guidelines.[102] One opportunity of hand hygiene counted as one observation. Results from the observations were entered into an observation form derived from WHO Hand Hygiene Guidelines.[102] The observations were conducted during February to April 2011.

iv. The questionnaire consisted of three parts: the first part was concerned with general information; the second part contained questions to assess current knowledge; and the last part contained questions to assess beliefs about hand hygiene following the TDF. Questions regarding personal knowledge were derived from hand hygiene knowledge questionnaires from the WHO guideline for hand hygiene. [30] Hand hygiene knowledge questionnaires had 8 scale items and scores between 0 and 25. Likert scales with five points were used to capture each participant's degree of agreement with a statement (1 = strongly disagree, 5 = strongly agree). There were 16 questions with these scale items and total scores could range between 16 and 80.

v. The focus group discussions made use of five open-ended questions to assess culture and group behavior of HCWs towards infection control and hand hygiene practice. The contents of the interviews covered five mains issues including: (i) current hand hygiene practice, (ii) reasons for performing hand hygiene, (iii) guidelines on hand hygiene, (iv) obstacles/barriers for hand hygiene practices, and (v) promotions or campaigns to improve hand hygiene.

vi. The semi-structured interviews consisted of six open-ended questions to assess obstacles to improving infection control and hand hygiene. The contents of the interview covered six mains issues: (i) effective infection control, (ii) knowledge about hand hygiene practice, (iii) attitude toward hand hygiene, (iv) resources, (v) organizational authority of hospital infection control department, and (vi) monitoring and feedback system on infection control.

vii. Hand hygiene observations were recorded in the observation form provided in the WHO guidelines for hand hygiene. [30]

Example questions of each form for capturing the 14 TDF domains are shown in Appendix C.2.

Data analysis

Analysis was performed for both the quantitative data (including data from questionnaire and observations) and for qualitative data (including data from focus groups and interviews).

Quantitative data

Descriptive statistics were used to describe general characteristics of HCWs' current knowledge and current hand hygiene practices. Estimates of internal consistency were calculated for theoretical domains and factors using Cronbach’s alpha with a cutoff of 0.60 which is considered sufficient for preliminary research.[171] Domain scores were based on responses measured on a five-point Likert scale. For negatively worded items, the scale scores were reversed. A mean score of each domain was used in the analysis. For identifying barriers and enablers to good hand hygiene practice, a low mean value was taken to suggest that a particular domain may be a barrier, and a high mean value was taken to suggest that it may be an enabler.

Pearson's correlation coefficients were used to assess correlations between domain scores; these were defined as weak (0.0 to 0.39), moderate (0.40 to 0.69), or strong (0.70 to 1.0).[172] All analysis was performed using STATA version 14.0 (StataCorp LP, College station, Texas).

Qualitative data

All text data were directly recorded by audiotape and by manual writing on forms. The recordings were transcribed verbatim and transcriptions verified prior to analysis. All the data were analyzed line-by-line until a clear sense of the relationship among the themes emerged. Content analysis was applied using the TDF themes for analysis.[173]

The set of transcript data was analyzed following six steps:

1) Coding and describing transcripts

   The 14 TDF domains[88] were taken from standard definitions (Appendix C.2) to classify "utterances" (coded interview quotes) from the transcript. The coding scheme was generated as guidance to ensure consistency in coding. Each transcript was coded into the 14 TDF domains.

2) Generating specific data

   Specific beliefs were generated for each utterance in all TDF domains. A specific belief is "a collection of participant responses with a similar underlying theme that suggests a problem and/or influence on the target behaviour".[88]

3) Identification of relevant theoretical domains

   Identification and classification of specific data into constructs of each TDF definition was performed.[91] The approach to identification was adapted from Bocart *et al.*, which used psychological theory to inform the choice of methods to implement a hand hygiene intervention.[97] An example question for each theoretical construct represented within each domain is presented in Table 4.1.

Table 4.1: The theoretical constructs used to analyses text data and example questions

Theoretical constructs represented within each domain [a]	Example questions to analyses text [b]
TDF 1: Knowledge	
Knowledge (including knowledge of condition /scientific rationale)	Can you describe the guidelines to perform proper hand hygiene?
Procedural knowledge	Can you discuss when to perform hand hygiene?
Knowledge of task environment	Can you describe why you should be performing hand hygiene?
	Can you describe how the IC team/ICWN works?
	Do you know what information the IC team/ICWN can collect?
TDF 2: Skills	
Skills	Can you explain the proper procedure of performing hand hygiene?
Skills development	
Competence	How easy or difficult is it to perform hand hygiene on your unit?
Ability	
Interpersonal skills	Can you describe how to use the ____?
Practice	Do you know how to respond when the IC team/ICWN reminds you?
Skill assessment	
TDF 3: Social/ professional role and identity	
Professional identity	What role will the IC team/ICWN play in enhancing hand hygiene?
Professional role	

[a] Theoretical constructs applied from Michie, *et al.* 2014.

[b] Example questions are adapted from Boscart, *et al.* 2012.

TDF = Theoretical Domains Framework; IC = infection control; ICWN = infection control ward nurse

Table 4.1: The theoretical constructs used to analyses text data and example questions (cont.)

Theoretical constructs represented within each domain [a]	Example questions to analyses text [b]
TDF 3: Social/ professional role and identity	
Social identity Identity Professional boundaries Professional confidence Group identity Leadership Organizational commitment	Do you think the IC team/ICWN should determine how you perform hand hygiene? Do you feel that the guidelines for performing hand hygiene with the IC team/ICWN are congruent with your professional standard of practice? Should proper hand hygiene be practiced at all levels of staff?
TDF 4: Beliefs about capabilities	
Self-confidence Perceived competence Self-efficacy Perceived behavioural control Beliefs Self-esteem Empowerment Professional confidence	How difficult or easy is it for you to maintain proper hand hygiene? What problems have you encountered when trying to practice proper hand hygiene? What would help you to increase hand hygiene compliance? How confident are you that you can increase compliance with the barriers and difficulties you face? How well equipped and comfortable do you feel in increasing your level of hand hygiene compliance? When using the IC team/ICWN? How capable do you feel in maintaining increased compliance with hand hygiene? When using the IC team/ICWN? How well will this the IC team/ICWN record your hand hygiene?

[a] Theoretical constructs applied from Michie, *et al.* 2014.

[b] Example questions are adapted from Boscart, *et al.* 2012.

TDF = Theoretical Domains Framework; IC = infection control; ICWN = infection control ward nurse

Table 4.1: The theoretical constructs used to analyses text data and example questions (cont.)

Theoretical constructs represented within each domain [a]	Example questions to analyses text [b]
TDF 5: Optimism	
Optimism Pessimism Unrealistic optimism Identity	Does HCW wash their hand every time required for hand hygiene?
TDF 6: Beliefs about consequences	
Beliefs Outcome expectancies Characteristics of outcome expectancies (physical, social, emotional) Anticipated regret Consequents	Does hand hygiene play an important role in your current practice? For yourself? For your patients? Can you explain why? Do you believe that the IC team/ICWN will play an important role in your practice? How will you feel if you are able to increase hand hygiene compliance? How will you feel if you do not? Do you foresee any positive or negative outcomes of increased hand hygiene compliance on patient outcomes? Staff outcomes? Do you foresee these outcomes/consequences as long term or short term? Do you foresee a negative consequence of using the IC team/ICWN? For patient outcomes? Staff outcomes? What do you think will happen if hand hygiene compliance is not increased in terms of patient outcomes? Staff outcomes? Do you think these are short- or long-term consequences?

[a] Theoretical constructs applied from Michie, *et al.* 2014.

[b] Example questions are adapted from Boscart, *et al.* 2012.

TDF = Theoretical Domains Framework; IC = infection control; ICWN = infection control ward nurse

Table 4.1: The theoretical constructs used to analyses text data and example questions (cont.)

Theoretical constructs represented within each domain [a]	Example questions to analyses text [b]
TDF 7: Reinforcement	
Rewards (proximal/distal, valued/not valued, probable/improbable)	Do you feel any reward / punishment can increase your hand hygiene compliance?
Incentives	
Punishment	
Consequents	
Reinforcement	
Contingencies	
Sanctions	
TDF 8: Intentions	
Stability of intentions	Would you like to increase your hand hygiene compliance?
Stages of change model	Do you feel a need to increase your hand hygiene compliance?
Transtheoretical model and stages of change	What are your reasons for increasing your hand hygiene compliance?
	Is there any aspect of your hand hygiene performance that you could improve on? Frequency, activity related?
	Are there other things that you would like to achieve that might interfere with increasing your hand hygiene compliance?
	Are there incentives to increasing hand hygiene compliance? If so, what are they?

[a] Theoretical constructs applied from Michie, *et al.* 2014.

[b] Example questions are adapted from Boscart, *et al.* 2012.

TDF = Theoretical Domains Framework; IC = infection control; ICWN = infection control ward nurse

Table 4.1: The theoretical constructs used to analyses text data and example questions (cont.)

Theoretical constructs represented within each domain [a]	Example questions to analyses text [b]
TDF 9: Goals	
Goals (distal/proximal) Goal priority Goal/target setting Goals (autonomous/controlled) Action planning Implementation intention	How will the IC team/ICWN increase hand hygiene compliance? Who needs to work differently for this to occur? When? Where? How do you know whether increased hand hygiene compliance has occurred? What do you currently do in term of performing hand hygiene? Is this new or existing behaviour that needs to become a habit? Can the context be used to prompt you to perform hand hygiene? (prompts: layout, reminders, equipment) How long do you think the changes are going to take?
TDF 10: Memory, attention and decision processes	
Memory Attention Attention control Decision making Cognitive overload/tiredness	Do you usually perform hand hygiene? How often on a regular shift? Do you consciously think and make the decision to wash your hands? What factors influence that decision? Type of care activity? Type of patient? Time? How much attention do you have to pay to perform hand hygiene?

[a] Theoretical constructs applied from Michie, *et al.* 2014.

[b] Example questions are adapted from Boscart, *et al.* 2012.

TDF = Theoretical Domains Framework; IC = infection control; ICWN = infection control ward nurse

Table 4.1: The theoretical constructs used to analyses text data and example questions (cont.)

Theoretical constructs represented within each domain [a]	**Example questions to analyses text** [b]
TDF 10: Memory, attention and decision processes	
	Do you remember to perform hand hygiene? How? Do you think the reminder system in the IC team/ICWN will enhance your hand hygiene? Can you think of times where you might not perform hand hygiene, such as competing tasks or time constraints?
TDF 11: Environmental context and resources	
Environmental stressors Resources/material resources (availability and management) Organisation culture/climate Salient events/critical incidents Person x environmental interaction Barriers and facilitators	Where do you disinfect your hands? Have you used a wearable alcohol dispenser device? How does this impact your hand hygiene performance? To what extent do physical or resource factors, such as the availability and functioning of wall units and technology, facilitate or hinder performing hand hygiene? Do you believe that the IC team/ICWN will enhance your hand hygiene performance?
TDF 12: Social influences	
Social pressure Social norms (subjective, descriptive, injunctive norms) Group conformity Social comparisons Group norms Power(hierarchy) Intergroup conflict	Does hand hygiene play an important role on your unit? Can you explain why? Do you believe that nursing staff on this unit are washing their hands when necessary? To what extent do social influences facilitate or hinder performing hand hygiene? Social influence from your peers? Will you or have you ever observed others performing hand hygiene?

[a] Theoretical constructs applied from Michie, *et al.* 2014.

[b] Example questions are adapted from Boscart, *et al.* 2012.

TDF = Theoretical Domains Framework; IC = infection control; ICWN = infection control ward nurse

Table 4.1: The theoretical constructs used to analyses text data and example questions (cont.)

Theoretical constructs represented within each domain [a]	Example questions to analyses text [b]
TDF 12: Social influences	
Social support (personal/professional/organizational, intra/interpersonal, society/community) Alienation Group identity Modelling	Managers? Other professional groups? Patients? Relatives? Do you believe that there will be social influences from your peers to use the IC team/ICWN? Managers? Patients? Other groups? Do you have role models in performing hand hygiene? Who?
TDF 13: Emotion	
Fear Anxiety Affect Stress Depression Positive/negative affect Burn-out	Does performing hand hygiene elicit an emotional response? If so, what? To what extent will emotional factors facilitate or hinder your hand hygiene? Do you believe that emotional factors will influence the use of the IC team/ICWN?
TDF 14: Behaviour regulation	
Self-monitoring Breaking habit Action planning	What initial steps need to be taken to improve hand hygiene compliance/ use the IC team/ICWN on an individual level? How about on an organizational level? Can you think of any procedures that would encourage increased hand hygiene compliance/ use of the IC team/ICWN?

[a] Theoretical constructs applied from Michie, *et al.* 2014.

[b] Example questions are adapted from Boscart, *et al.* 2012.

TDF = Theoretical Domains Framework; IC = infection control; ICWN = infection control ward nurse

4) Connecting and interrelating data

Following identification of the relevant theoretical domains, the beliefs were mapped for systematically analyzing interrelations within the behavioural domain into the COM-B system proposed by Michie *et al.*, which considers capability, opportunity and motivation as all determining behaviour[37] (Table 4.2). This framework was validated for use in behaviour change and implementation research by Cane *et al.*[88] Capability, which includes having the necessary knowledge and skills, is defined as “the individual's psychological and physical capacity to engage in the activity concerned”.[37] Motivation is defined as “all those brain processes that energize and direct behaviour, not just goals and conscious decision-making”.[37] It includes “habitual processes, emotional responding, as well as analytical decision-making”.[37] Opportunity is defined as “all the factors that lie outside the individual that make the behaviour possible or prompt it”.[37]

Table 4.2: Mapping of the Behaviour Change Wheel's COM-B system to the TDF Domains, from Cane *et al.,* 2012.[88]

COM-B component	**TDF Domain**	
Capability	Psychological	Knowledge
		Skills
		Memory, Attention and Decision
		Behavioural Regulation
	Physical	Skills
Opportunity	Social	Social Influences
	Physical	Environmental Context and Resources
Motivation	Reflective	Social/Professional Role & Identity
		Beliefs about Capabilities
		Optimism
		Beliefs about Consequences
		Intentions
		Goals
	Automatic	Social/Professional Role & Identity
		Optimism
		Reinforcement
		Emotion

5) Interpretation, creating explanatory results

Through the following steps, the set of psychological theories and models was used to represent the constructs from the relevant domains for understanding factors associated with non-compliance behaviour for hand hygiene. The interpretation was given for individual, team, and organizational levels, (Table 4.3) that were likely to influence hand hygiene behaviour of HCW. This identification was important in further steps to design the potential intervention , and based on construct allocations proposed by Michie *et al*.[42]

Table 4.3: Constructs in four theoretical domains, illustrating individual, team, and organizational levels, based on construct allocations reported by Michie *et al.*, 2005.[42]

Domain	Level		
	Individual	**Team**	**Organizational**
Environmental Context and Resources	Environmental stressors Person × environment interaction	Environmental stressors	Resources/material resources (availability and management)
Social Influences	Social support Social pressure	Leadership Social comparisons	Organizational climate/culture Change management

4.3 Results

Results are presented in seven parts:

1) Sample characteristics
2) Current knowledge about hand hygiene
3) Current hand hygiene practices
4) Perceived barriers for non-compliance with hand hygiene
5) Current beliefs about hand hygiene behaviour
6) Summary of relevant domain findings by applying the TDF
7) Mapping domain findings to the Behaviour Change Wheel's COM-B system.

4.3.1 Sample characteristics

Population

All 2,030 HCWs at the hospital were contacted to participate in this part of the study. Agreement was obtained from 1,694 (83.4%) participants who completed the self-administered questionnaire. Of these 1,582 participants were included in the analysis concerning current knowledge, current beliefs, and self-reporting about hand hygiene, while 112 participants were excluded due to incomplete the enrollment set (10 of them signed the informed consent form without completing the questionnaire, 8 of them completed the questionnaire without signing the consent form, and 94 of them did not complete both the questionnaire and the consent form).

Sample of the self-administered questionnaire

Of 1,582, almost half the participants completing the self-administered questionnaire were nurses (47.8%). The rest were auxiliaries (26.9%), nursing students (18.0%), and physicians (7.2%). 1,295 (81.9%) were female and 272 (17.19%) were male. The median number of years participants had spent working at the hospital was 7 (interquartile range [IQR] 2-16 years, range 0–45 years) Characteristics of study population are presented in Table 4.4.

Direct observation of hand hygiene practice

A total of 364 participants were randomly observed to assess current hand hygiene practice. Most observed HCWs were female (70.9 % [258/367]), and registered nurses (32.4% [118/364]). They were distributed across the hospital departments (medicine, surgery, paediatric, and obstetrics and gynecology), and roles (staff physician, registered nurse, nurse aides, medical student, nursing student, and visitor). Half of the observed staff worked in ICU wards (162/364). Mean work year experience in this hospital was 10.2 (IQR 3-14, range 1-27).

Sample of the focus group discussion

A total of 60 participants were approached to participate in six sessions of the focus group discussion, and 32 were recruited for four sessions. The distribution across the hospital, specialties (medicine, surgery), and roles (staff physician, registered nurse, infection control ward nurse, nurse aides) were intentionally representative of each type of HCWs by using of purposive sampling (Appendix C.3). Most participants were female (81.3 % [26/32]) (Table 4.5). Focus group discussions ranged in duration from 55 to 112 minutes, with a mean focus group discussion time of 74 minutes.

Sample of the semi-structured interviews

A total of 10 participants were approached for semi-structured interviews. From these five key informants were recruited. This included key administrators in the hospital including the hospital director and heads of department (medicine, surgery, laboratory) (Appendix C.4). Most participants were male (80.0 % [4/5]). Semi-structured interviews ranged in duration from 45 to 128 minutes, with a mean semi-structured interview time of 64 minutes.

4.3.2 Current knowledge about hand hygiene

All recruited HCWs who completed the self-administered questionnaire were assessed for current knowledge about hand hygiene. The median score for questions about knowledge of hand hygiene was 14 correct answers (IQR 13-16 items, range 0–22) out of a maximum of 25, and the mean knowledge score was similar in different HCW groups. Current knowledge of all participants derived from the questionnaire is presented in Figure 4.1 and Appendix C.5.

Table 4.4: Characteristics of the study population

	Categories of respondents				
	Physicians	**Nurses**	**Auxiliaries**	**Nursing students**	**Total**
N of respondents	13	812	458	299	1,582
Male n	8	42	183	39	272
Female n	5	770	275	260	1,310
Median work experience in this hospital in years [range] *	9.7 [1-22]	13.4 [1-44]	12.4 [1-45]	1.4 [0-4]	10.9 [0-45]
ICU n *	-	254	116	-	370
Non-ICU n *	-	471	307	-	778
Department of Eye Ear Nose Throat n *	-	32	23	-	55
Department of Obstetrics and Gynecology n *	-	130	73	-	203
Department of Medicine n *	-	165	94	-	259
Department of Paediatrics n *	-	119	76	-	195
Department of Surgery n *	-	363	189	-	552

N = number of respondents of total study population, n = number of respondents in subgroup of study population, ICU = Intensive-care unit

*Information is missing in these items

Table 4.5: Descriptive data for focus group participants (n = 32)

Focus group No.	n	Gender	Age (years)[a]	Length of service [b]	Role type	Work area	Work status
FG1	10	10 Females	31 [23-41]	6 [1-11]	Infection control ward nurses	5 ICU 5 Non-ICU	Full-time
FG2	10	1 Male 9 Females	29 [21-40]	3 [0-8]	Registered nurse	5 ICU 5 Non-ICU	Full-time
FG3	9	3 Males 6 Females	40 [30-55]	10 [3-14]	Nursing Assistant	4 ICU 5 Non-ICU	Full-time
FG4	3	2 Males 1 Female	32 [30-37]	5 [3-8]	Nurse aids	2 ICU 1 Non-ICU	Full-time

n = number of participant of part of study population, ICU = Intensive-care unit

[a] Median age in years [range]

[b] Median length work experience in this hospital in years [range]

4.3.3 Current hand hygiene practices

Current hand hygiene practices were assessed in two parts: i) self-reporting on hand hygiene practice from the questionnaire survey, and ii) current hand hygiene practice from direct observation.

Self-reporting on hand hygiene practice from questionnaire survey

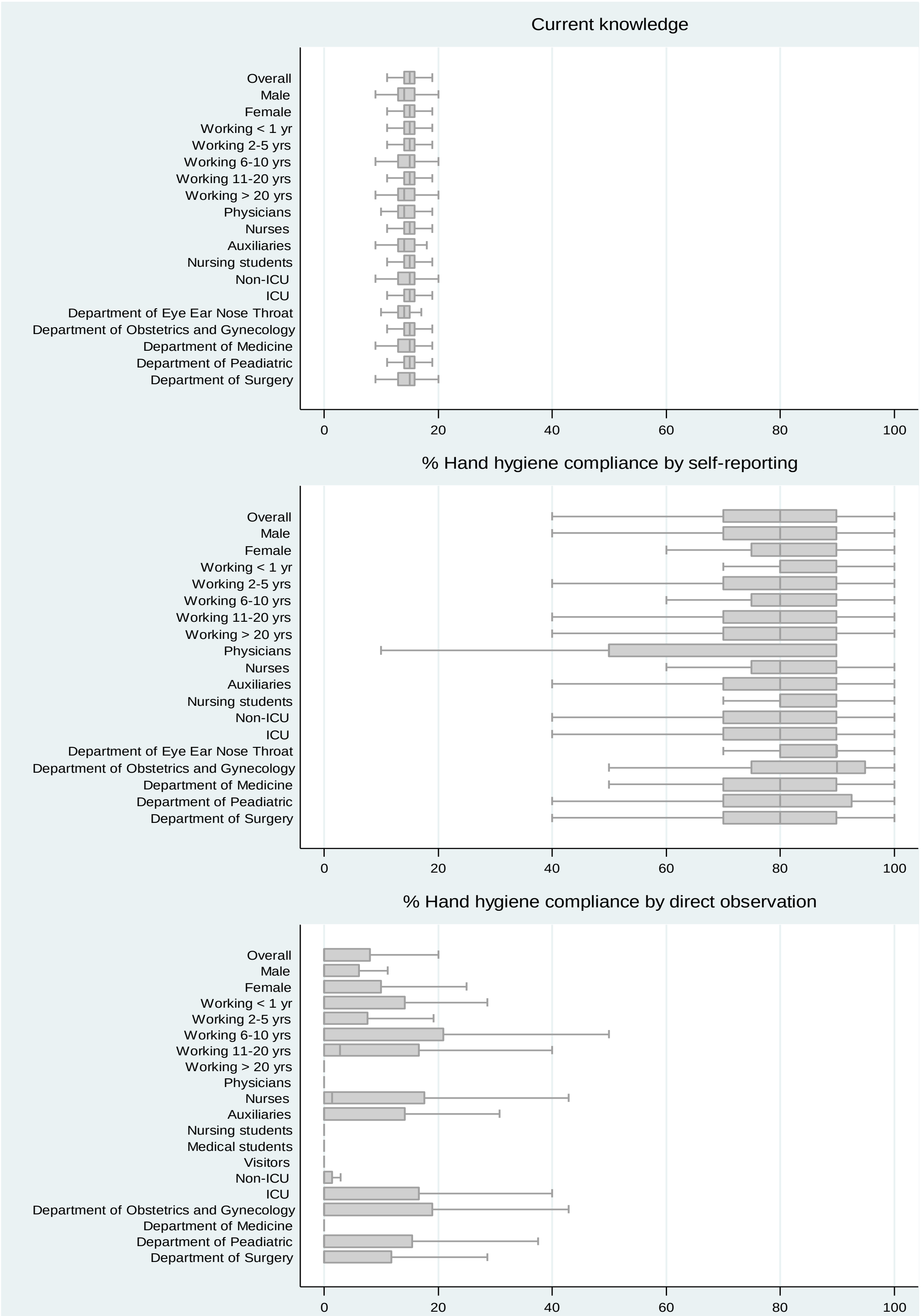
Out of 1,582 HCWs who completed self-administered questionnaires, only 1,126 completed the section on self-reporting of hand hygiene practice. The median self-reported hand hygiene compliance was 80% (IQR 70-90%, range 0–100%), and was similar for most categories of HCW. Physicians had the lowest self-reported compliance with a median of 50%. (Figure 4.1 and Appendix C.6)

Current hand hygiene practices from direct observation

Intra-rater reliability between observers was assessed before collecting the data, and the agreement was at a level of 0.73, which can be interpreted as substantial.[170]

Out of a total of 3,564 recorded hand hygiene opportunities from 364 HCWs hand hygiene was observed in 475 (13.3%). Hand hygiene was considered to have been performed correctly in 318 (8.9%) opportunities and incorrectly in 157(4.4%). Amongst opportunities where hand hygiene was performed, the percentage of correct hand hygiene practice was 66.9% (318/475). The median hand hygiene compliance was 0% (IQR 0-8.01%, range 0–100%). The indication associated with the lowest compliance was "*after touching patient surroundings"* (38/3,564), while the highest compliance was "*after body fluid exposure/ris*k" (610/3,564). HCWs, who did not use gloves during patient care (155/184), were more likely to perform hand hygiene correctly than HCWs who had been wearing gloves during patient care (59/113). The number of beds in the observation ward was negatively associated with compliance (Appendix C.9).

Figure 4.1: Score of current knowledge (n = 1,582) (top panel), % hand hygiene compliance by self-reporting (n = 1,126) (middle panel), and % hand hygiene compliance by direct observation (n = 364) (bottom panel) by explanatory variables



Absence of hand hygiene was not found to be associated with any individual HCW characteristics. Hand hygiene practice using alcohol hand rub was much more likely to be performed correctly than hand hygiene using soap and water. Handrubing was more often performed correctly than handwashing (155/184 vs. 163/291). Male sex was associated with poorer adherence to recommended hand hygiene practices (Appendix C.7).

Of 364 HCWs for whom at least 1 (range 1-55) hand hygiene opportunity was observed, 248 (68.1%) were never observed to perform hand hygiene and only 116 (31.9%) performed hand hygiene at least once. The mean hand-hygiene compliance in HCWs was 8.9% (IQR 0-8.0%, range 0–100%).

Observations of hand hygiene practices are presented in Figure 4.1, Table 4.6, Appendix C.7, and Appendix C.8.

Comparing hand hygiene practice between self-reporting and direct observation

Hand hygiene compliance from self-reporting and direct observation showed a lack of consistency (Appendix C.6 and Appendix C.8). Self-reported compliance was nearly 10 times higher than the compliance from direct observation (Appendix C.8). Comparisons of current hand hygiene by direct observation and self-reporting are presented in Figure 4.1.

Table 4.6: Summary of hand hygiene performance for all opportunities requiring hand hygiene (n = 3,564)

	Hand hygiene practices			
	Not performed n (%)	**Performed incorrectly n (%)**	**Performed correctly n (%)**	**Total n (%)**
Overall	3,089 (86.7 %)	157 (4.4 %)	318 (8.9 %)	3,564 (100 %)
Time period				
Morning	2,188 (87.6 %)	75 (4.4 %)	235 (9.4 %)	2,498 (100 %)
Afternoon	901 (84.5 %)	82 (4.4 %)	83 (7.8 %)	1,066 (100 %)
Indication				
Before touching a patient	654 (91.7 %)	11 (1.5 %)	48 (6.7 %)	713 (100 %)
After touching a patient	656 (88.1 %)	18 (2.4 %)	71 (9.5 %)	745 (100 %)
Before clean/aseptic procedures	449 (84.6 %)	20 (3.8 %)	62 (11.7 %)	531 (100 %)
After body fluid exposure/risk	426 (69.8 %)	85 (13.9%)	99 (16.2 %)	610 (100 %)
After touching patient surroundings	904 (93.7 %)	23 (2.4%)	38 (3.9 %)	965 (100 %)
Number of total beds				
8 beds	930 (80.5 %)	67 (5.8 %)	158 (13.7 %)	1,155 (100 %)
14 beds	155 (86.6 %)	13 (7.3 %)	11 (6.2 %)	179 (100 %)
30 beds	1,266 (89.0 %)	52 (3.7 %)	104 (7.3 %)	1,422 (100 %)

4.3.4 Perceived barriers for non-compliance with hand hygiene

Possible barriers for non-compliance identified in an open question on the questionnaire are reported in Table 4.7. HCWs reported irritation on hands after performing hand hygiene (25.7%), and some respondents suggested adding some ingredients in the hand hygiene product to reduce the irritation. This issue was also expressed in the focus group discussions. Another theme from these discussions was that lowered hand hygiene performance could arise due to allergies to alcohol in some HCW. The view was expressed that the hospital should provide other products for hand hygiene considering the allergic factors. Lack of hand washing supplies (24.8%) and emergencies in the workplace (17.3%) were cited as the most important barriers were reported.

Table 4.7: Perceived barriers for non-compliance with hand hygiene reported by respondents (N = 1,582)

Barriers	n (%)
Irritation on hands after performing hand hygiene	460 (25.7)
Lack of hand washing supplies such as towel, soap, alcohol handrub including irregular water supply	393 (24.8%)
Emergency in workplace	273 (17.3%)
No facility for hand washing such as sink	261 (16.5%)
Lack of time (overburdened by work) or staff shortages	230 (14.5%)
Dislike the hand washing supplies such as alcohol hand rub (locally made) , soap	173 (10.9%)
Misunderstanding on glove use	64 (4.1%)
Lack of administrative sanction of non-compliers or rewarding of compliers to perform hand hygiene	29 (1.8%)
Lack of scientific knowledge regarding impact of hand hygiene on hospital-acquired infection	25 (1.6%)
Lack of role model from colleagues or superiors	16 (1.0%)

4.3.5 Current beliefs about hand hygiene behaviour

This section summarizes the findings concerning beliefs about hand hygiene behaviour (derived from the opinion survey of the questionnaire on = 1,582). The questions regarding personal beliefs about hand hygiene following the TDF covered the following 12 domains: knowledge; skills; social/professional role and identity; beliefs about consequences; beliefs about capability; intentions; goals; memory, attention, and decision processes; environmental context and resources; social influences; emotion; and behavioural regulation. Optimism and reinforcement domains were excluded because in a systematic review of hand hygiene using a theoretical behavioural approach information was not reported on these two domains. [100]

The internal consistency measures (Cronbach's α) ranged between 0.64 - 0.69: knowledge = 0.69; skills = 0.65; social/professional role and identity = 0.68; beliefs about consequences = 0.64; intentions = 0.66; goals = 0.65; memory, attention, and decision processes = 0.65; environmental context and resources = 0.66; social influences = 0.64; emotion = 0.64; and behavioural regulation = 0.64.

The mean scores of each theoretical domain ranged from 2.58 to 4.86: knowledge = 4.14; skills = 3.67; social/professional role and identity = 2.58; beliefs about consequences = 4.66; beliefs about consequences = 4.46; intentions = 4.86; goals = 4.74; memory, attention, and decision processes = 4.55; environmental context and resources = 4.75; social influences = 3.81; emotion = 4.27; and behavioural regulation = 3.83. (Appendix C.9).

Reflecting the beliefs about hand hygiene behaviour, the *"intentions"* domain was reported to be the highest among all HCWs (4.86; 95% confidence interval [CI] 4.84 to 4.88), while the *"social/professional role and identity"* domain was reported to be the lowest among all HCWs (2.58; 95% CI 2.55 to 2.63).

4.3.6 Summary of relevant domain findings by applying the TDF

The relevant domain findings were summarized from qualitative data (from focus group discussion and semi-structured interviews) and quantitative data (questionnaires and direct observations). The results of this are presented in two parts: i) summarizing results by relevant theoretical domains, and ii) summarizing interrelations between the relevant domains.

Relevant theoretical domains

The fourteen domains of TDF identified from the two data sources as relevant to HCW hand hygiene compliance included: (1) knowledge; (2) skills; (3) social/professional role and identity; (4) beliefs about capabilities; (5) optimism; (6) beliefs about consequences; (7) reinforcement; (8) intentions; (9) goals; (10) memory, attention and decision processes; (11) environmental context and resources; (12) social influences; (13) emotion; and (14) behavioural regulation. Examples of specific beliefs from semi-structured interviews and focus group discussions are presented in Table 4.8.

Table 4.8: Examples of specific beliefs elicited from semi-structured interviews with key informants (n=5) and focus group discussions with representative of each type of healthcare worker (n=32)

Domain/ Construct	Specific beliefs	Example quotation
Knowledge		
-Knowledge of condition /scientific rationale	I believe that nurse aides and ancillary staff still did not know the link between improving hand hygiene practices and the impact of hospital-acquired infection	*"…. nurse aides and* ancillary staff*, they still did not know the impact of hospital-acquired infection…. In monthly reports we routinely report about the case of hospital-acquired infection and impact of improving hand hygiene practices…. They did not understand this point yet…."*
	Nurse aides do not understand how to interpret current presentation of hospital-acquired infections on the ward	*"…current presentation of HAI, it is difficult to understand for nurse aides group… just show the graph in different color but they did not understand how to interpret it"*
-Procedural knowledge	I do not know which hand hygiene product should be used in each activity and how different to use each product	*"…. yes, we (nurse aids) did not know which hand hygiene product should be used in each activity and how to use each different product. We normally use the products that we have, I quite to use plain soap…."*
-Knowledge of task environment	I am aware of hand hygiene practices before and after touching patient, because it helps to prevent cross-transmission of pathogens between people	*"…. before and after touching we should wash our hands…. We wash because it helps to prevent cross-transmission of pathogens between people and it helps to protect us from getting pathogens ourselves…."*

Table 4.8: Examples of specific beliefs elicited from semi-structured interviews with key informants (n=5) and focus group discussions with representative of each type of healthcare worker (n=32) (cont.)

Domain/ Construct	Specific beliefs	Example quotation
Skills		
-Skills development	Posters give correct steps of hand hygiene practice. We perform correctly hand hygiene practice by looking at posters every time	*"…. (Posters) shows us how correct steps of hand washing. It helps in the memory, if we see it every time of hand washing. Then we do following these steps every time, we will do correctly in all steps."*
-Competence	I did not know how it is properly clean when I perform hand hygiene practice	*"….How do we (nurse aides) know it's properly cleaned…."*
-Practice	I believe that workers will miss steps of hand hygiene practices because they think they have little physical contact with patients.	*"…. from our (ICWNs) observation, for several type of workers, such as auxiliaries, they have few activities that involve directly touching patients. They quite often touch the environment surrounding the patient…. then they will miss steps of hand hygiene practices"*
-Skill assessment	I believe that proper hand hygiene is difficult to measure	*"…. in this issue (correct of hand hygiene practice), it is difficult to measure…."*
	ICWNs try to immediately feedback to ward staff when they face the incorrect practice of hand hygiene and give teaching for proper hand hygiene practice	*"…. really we (ICWNs) try to immediately tell them (other staff) that you do it is wrong practice, then we will teach what correct practice for hand hygiene is. You should do again following all steps of hand hygiene practices…."*

Table 4.8: Examples of specific beliefs elicited from semi-structured interviews with key informants (n=5) and focus group discussions with representative of each type of healthcare worker (n=32) (cont.)

Domain/ Construct	Specific beliefs	Example quotation
Skills		
-Skill assessment	I believe that quality of hand hygiene practice of individual HCW is difficult to measure. They just wash their hands until feeling clean	*"....for the quality of hand hygiene practice of individual HCW (lough)....it is difficult to measure.... they just wash hands, they feel clean enough"*
Social/ professional role and identity		
-Professional identity	ICWNs try to immediately provide feedback when improper hand hygiene practice is occurring	*"....really we (ICWNs) try to immediately tell them (other staff) that what you do it is wrong practice, then we will teach what correct practice for hand hygiene is. You should do it again following all steps of hand hygiene practices...."*
-Professional role	All HCWs know when they should perform hand hygiene but they did not perform hand hygiene 100% of the time. Even nurses did not perform hand hygiene practice every time before doing aseptic procedures.	*".... they (all HCWs) know, they should wash their hands. But it is not 100 % to perform hand hygiene in practice, even nurses they must wash their hand when they will do aseptic procedure...."*

Table 4.8: Examples of specific beliefs elicited from semi-structured interviews with key informants (n=5) and focus group discussions with representative of each type of healthcare worker (n=32) (cont.)

Domain/ Construct	Specific beliefs	Example quotation
Social/ professional role and identity		
-Professional role	Hand hygiene is a standard part of my patient consultations	*"Every month, ICWN will report information about HAI and make discussion with all ward staff to solve the problem."*
-Professional boundaries	Hand hygiene is not specific to just my specialty. Hand hygiene should be performed by everyone	*"Information about HCAI, such as name of pathogen, cost of treatment, is presented monthly at our ward meeting, and it has resulted in improving behaviour of HCWs for a few days after meeting then they do the same practice. After notifying this issue, we will get more co-operative behaviour from a group of registered nurse than from a group of nurse aides.… because they did not understand how it involve them…. "*
-Organizational commitment	ICWN should routinely asses knowledge of all HCWs	*"….we have ICWN in every ward, if the hospital has enough budget to support, in every year we should routinely test knowledge of ward staff then we will get baseline results …. We should test again 3 months later for monitoring the changing trend…."*
Beliefs about capabilities		
-Self-confidence	I am confident that nurses do hand hygiene quite often after caring the patient	*"…. In general, for nurses… especially nurses who have activity to directly contact patient such as touching a patient, taking bed bath…. They will do more cleanly for hand washing…"*

Table 4.8: Examples of specific beliefs elicited from semi-structured interviews with key informants (n=5) and focus group discussions with representative of each type of healthcare worker (n=32) (cont.)

Domain/ Construct	Specific beliefs	Example quotation
Beliefs about capabilities		
-Perceived competence	Some HCW groups have inferior hand hygiene performance than other groups	*"....under my observation, several type of HCWs performed hand washing....but hand washing is done less in group of hospital support staff, because they have less activities that require contact with the patient…. they occasionally perform hand washing as normal habit, and they do not know the corrected steps of hand washing…. they do not look at the poster as well…. "*
-Beliefs	I believe that actual hand hygiene practice is only hand washing with antiseptic soap	*".... Actual hand hygiene practice is only hand washing with antiseptic soap…."*
	Alcohol-based handrub was preferable for using when HCWS do not feel their hands are dirty	*"....but most HCWs will use alcohol-based handrub…. And if they feel it is not dirty then they will not wash their hands…."*
-Empowerment	Belief that without visual reminders (e.g. posters) HCWs may not remember to perform the correct steps of hand hygiene	*"....these posters were placed at almost all sinks…. it is helpful for following steps of hand washing…"* *"…. it is easily to guide the patients….we recommended patients to do hand washing following the steps that show this as well.…"*

Table 4.8: Examples of specific beliefs elicited from semi-structured interviews with key informants (n=5) and focus group discussions with representative of each type of healthcare worker (n=32) (cont.)

Domain/ Construct	Specific beliefs	Example quotation
Optimism		
-Optimism	Only proper hand hygiene can effectively prevent HCAI	*"….hand washing must be performed at the correct time and with the correct steps for effective HAI prevention …."*
-Pessimism	Overall hand hygiene compliance is 70 % but incomplete adherence to hand hygiene guidelines in the steps performed	*"Overall HCW's hand hygiene is certainly 70 percent compliance that it is correct…. but all steps of hand washing maybe not completely followed."*
-Identity	Hand hygiene is performed well, if only for self-protection	*"….they certainly performed proper hand washing before going back home for protecting themselves…. but during working shift, I am not sure…."*
	Gloves can replace hand hygiene practice because it takes too long to wash hands	*" ….when I am waiting long queue to wash my hand, I will use glove, because after discarding glove there is no need to wash hands , then I can continue to take care of another patients."*
Beliefs about consequences		
-Beliefs	Quality of hand hygiene is difficult to tell, while overall compliance of our ward is a round 70 %	*"…. Overall compliance of our ward is around 70 percent. And for quality of hand washing, it is difficult to measure…. they just wash their hands, and they say it is clean enough …."*
-Outcome expectancies	Proper hand hygiene is effective at protecting HCWs and patients from infections	*"….must be washed in proper hand hygiene practice, then it will be effective to protect themselves and patients. …. but in general they do not wash"*

Table 4.8: Examples of specific beliefs elicited from semi-structured interviews with key informants (n=5) and focus group discussions with representative of each type of healthcare worker (n=32) (cont.)

Domain/ Construct	Specific beliefs	Example quotation
Beliefs about consequences		
-Characteristics of outcome expectancies (physical, social, emotional)	I believe that I will not wash my hands when they feel less dirty	*"If my hand is less dirty then I will not wash my hands"*
-Anticipated regret	I believe that overall hand hygiene compliance of staff is more than 80%, but they perform incorrectly.	*"….as I evaluate it, I think, overall compliance of our staff is okay, it is over more than 80 percent…. in general, they wash not completely all steps of recommendation."*
	If the goal of making hand hygiene part of routine habit could be attained, then hand hygiene would be performed automatically	*"If they make hand hygiene practice as normal habit, then they will do automatically."*
Reinforcement		
-Rewards	Rewards for good ICT work have been provided in the past but not in the most recent years	*"….in last several years we have had infection control meetings annually , and rewards for good infection control team work were provided, but the meeting was skipped in later year "*

Table 4.8: Examples of specific beliefs elicited from semi-structured interviews with key informants (n=5) and focus group discussions with representative of each type of healthcare worker (n=32) (cont.)

Domain/ Construct	Specific beliefs	Example quotation
Reinforcement		
-Reinforcement	Hand hygiene compliance could be improved by setting a competition in the hospital ward and providing the reward	*"We should set a competition on hand hygiene between the wards in our hospital and also provide the reward. Because staff of each ward love their own ward as home, they don't want to have a bad image for their ward "*
Intentions		
-Stability of intentions	Intention to completely perform all hand hygiene steps was lacking because of the time this would consume	*"….no , we quite do not complete all steps of hand hygiene practice because it take so long time to do until complete all steps (laughs)…."*
-Stages of change model	They intend to wash their hands after taking care of the patient with a bed bath	*"….every time, they will play attention to wash their hands after taking bed bath for patient…."*
Goals		
	Hand hygiene knowledge and training are a necessity	*"New intern students must be taught how to perform hand hygiene until correctly performing, before starting the activity of nursing."* *"New staff must have basic knowledge about hand hygiene recommendation, and they must perform correctly."*

Table 4.8: Examples of specific beliefs elicited from semi-structured interviews with key informants (n=5) and focus group discussions with representative of each type of healthcare worker (n=32) (cont.)

Domain/ Construct	Specific beliefs	Example quotation
Goals		
	When taking all priorities into considerations, hand hygiene is first priority	*"…. firstly for new staff, we will teach hand hygiene practice, until they do correctly all steps of hand washing.…"*
	If the goal of making hand hygiene part of routine habit could be attained, then hand hygiene would be performed automatically	*"If they make hand hygiene practice as normal habit, then they will do automatically."*
Memory, attention and decision processes		
	Reminders are useful for my hand hygiene practice	*"…. It (poster) is helpful. It presents the hand washing steps, if we look at this every day. It will make memory.…"*
	Not practicing hand hygiene is a conscious decision and decisions not to wash hands may result from a lack of awareness about benefits and the fact that it is perceived to be impractical	*"…. a lot of people, they know, when they should wash their hands, but they did not wash because they are less aware.… hand hygiene is not important, hand hygiene is not useful, it is impractical.… benefits of hand hygiene are beyond themselves.…"*

Table 4.8: Examples of specific beliefs elicited from semi-structured interviews with key informants (n=5) and focus group discussions with representative of each type of healthcare worker (n=32) (cont.)

Domain/ Construct	Specific beliefs	Example quotation
Memory, attention and decision processes		
	AHR was used instead of handwashing because it was quicker	*"…. When we need to quickly clean hands, the AHR was used instead before nursing care."* *"…if we are working in rushed period when we have less time to spend in hand hygiene practice we will apply alcohol-based handrub…."*
	An easily visible hand hygiene station makes it easier to remember to practice hand hygiene. AHR is perceived to be a second choice option.	*"…. when they look at towel shelf, they saw, it has no towel supply…. in several people, they will use AHR instead…."*
Environmental context and resources		
	When I am busy, I am less likely to comply with hand hygiene guidelines	*"…. during day shift, it is so busy….it is difficult to do this, but I try to do as I can …."*
	Easy access to hand hygiene stations makes it easier to practice hand hygiene.	*"…. Another factor is lack of towels to use…."* *"….especially during shift turning between night and day shift, towels are required more to use…. but it is difficult to manage to proper supply…."* *"The problem is…. there are not enough towels…."*

Table 4.8: Examples of specific beliefs elicited from semi-structured interviews with key informants (n=5) and focus group discussions with representative of each type of healthcare worker (n=32) (cont.)

Domain/ Construct	Specific beliefs	Example quotation
Environmental context and resources		
	Availability of towels where they are needed may limit ability to perform hand hygiene.	*"…. when they look at the towel shelf, they saw, it has no towel supply, then they will not do completely all steps of hand washing…. they feel, it no needs to be done completely.…"*
		"We support all resources for hand washing, I am confident we have enough supplies. But they fail to manage accountability in some wards "
Social influences		
	Other team members influence my hand hygiene practice	*"….every time when hospital has a campaign to improve hospital quality, they will improve hand hygiene practice as well…."*
		"They will do well, if it is on period of promoting hand hygiene."
		"Every month, ICWN will report information about HCAI and make discussions with all ward staff to solve the problem."
		"If you can improve hand hygiene in doctors, then we will wash as well"
		"when ICT come to the ward we will do more or might have less activity so have less required hand hygiene"

Table 4.8: Examples of specific beliefs elicited from semi-structured interviews with key informants (n=5) and focus group discussions with representative of each type of healthcare worker (n=32) (cont.)

Domain/ Construct	Specific beliefs	Example quotation
Social influences		
	Other team members influence my hand hygiene practice	*"ICWN of the ward regularly feedback on hand hygiene to ward staff, but some staff were ignore because they found incorrect practice from ICWNs as well "*
Emotion		
	More concerned with hand hygiene practice because of fear to carriage pathogens back to home	*"….they will fear to get pathogens from touching the patient and bring pathogens to their family so that every staff will concentrate more to clean their hands before going back home…."*
	Due to lack of towel at sink , I feel lazy to perform hand hygiene	*"If I wash without towel, I could not wash. I fell lazy for waiting long queue, but it has no towel to use…."*
Behaviour regulation		
	Hand hygiene practice of staff was monitored periodically by the ICWN	*"Hand hygiene practice of our ward staff was evaluated periodically by ICWN."* *"….It's going to have an evaluation form, it was evaluated periodically (hand hygiene practice) …."* *"….under my observation….hand washing is done less in group of hospital support staff, because they have less activity to contact the patient…. if they occasionally perform hand washing as normal habit, and they did not know the corrected steps of hand washing…. they did not look at the poster as well…then I will said loudly,…Um…. please wash your hands in the correct steps "*

TDF 1: Knowledge

The knowledge domain considered knowledge of condition/scientific rationale, procedural knowledge, and knowledge of task environment.

From the questionnaire to assess the level of knowledge about hand hygiene similar results were found for different types of HCWs and different departments (Figure 4.1), while the questionnaire survey indicated high agreement that the "knowledge" domain (4.41, 95% CI 4.09 to 4.18) had an impact on hand hygiene behaviour. Selecting an improper product for hand hygiene was commonly seen in the observations and may reflect lack of knowledge.

In the focus group of ICWNs, lack of knowledge about scientific rationale for hand hygiene was found in a group of auxiliaries. While, in the focus group of nurse aides, participants said that they knew why they should wash their hands (i.e. because proper hand hygiene helped to eliminate cross-transmission between HCW and patient), but they did not know what criteria to use for selecting appropriate hand hygiene products.

In all of the focus groups, almost all HCWs claimed to have enough procedural knowledge, knowing when they should wash their hands and how many steps there were in correct hand hygiene practice. But a common theme was that not all steps of hand hygiene practice were followed. In some cases, this may have been because of emotional factors (i.e. if having a feeling of "not dirty" after touching a patient, then the HCW would be likely to not perform hand hygiene or perform incomplete steps of hand hygiene. Conversely, if having a feeling of "dirty" after performing an aseptic procedure, then an HCW would be more likely to concentrate to perform hand hygiene practices). Focus group participants expressed the view that aseptic procedure for treatment was strongly related to performance of hand hygiene practice in nurse groups, and touching the environment of patient was weakly related to hand hygiene practices in groups of auxiliaries.

From the semi-structured interviews, most key administrators expressed confidence that all HCWs had proper knowledge about hand hygiene guidelines, but believed that they often ignored hand hygiene in practice. Only one key administrator mentioned that knowledge of hand hygiene amongst HCWs needed to improve. While similar results were found in focus groups of ICWNs, this group suggested that improving knowledge in hand hygiene practice of HCWs by setting routine knowledge assessments for all HCWs.

Almost all HCWs have enough knowledge of a condition to clean their hands but they did not do every time as required, because emotional concepts of "dirtiness" and "cleanliness" of each nursing activity were used as criteria to perform hand hygiene. When finishing activities involving the patient, however, it does matter that activity was high or low risk activity. If HCW have this feeling of dirtiness, then they will perform hand hygiene, and if they feel this cleanliness, then they will not perform hand hygiene.

TDF 2: Skills

The skills domain includes skills, skills development, competence, ability, interpersonal skills, practice, and skill assessment.

From the questionnaire, there was moderately high agreement that the "skills" domain (3.67, 95% CI 3.62 to 3.73) had an impact on hand hygiene behaviour, while hand hygiene observations showed hand hygiene was often performed with incomplete steps and this could be considered as indicating lack of skills.

In the focus group discussion, lack of skills to assess proper hand hygiene was found in a group of nurse aides. Similar results were found from a group of ICWNs. ICWNs try to give feedback immediately to staff when wrong hand hygiene practice is found.

In the semi-structured interviews, the need to improve skills was raised. The view was expressed that while all staff perform hand hygiene, many perform it incorrectly. Staff also expressed a belief that proper hand hygiene is difficult to measure.

TDF 3: Social/ professional role and identity

The domain of social/ professional role and identity covered professional identity, professional role, social identity, identity, professional boundaries, professional confidence, group identity, leadership, and organizational commitment.

From the questionnaire, there was moderately low agreement that the “skills” domain (2.58, 95% CI 2.52 to 2.63) had an impact on hand hygiene behaviour. It was also suggested that HCWs might try to do less activity with the patients when the ICT were performing hand hygiene observations because of concerns about the feedback the ICT would provide.

The focus group discussions generally revealed high professional confidence from all HCWs but less confidence in hand hygiene practices. This was because those joining the discussions did not feel sure about the quality and consistency of hand hygiene practice among HCWs, due to several reasons including individual (knowledge, forgetfulness, awareness) and social contexts (less supplies, staffing, high workload, urgent work).

The role of ICWNs was thought to be clearly identified and the ICWN was expected to be a key player to promote hand hygiene in each ward. Difficulties to act in the role of ICWN were also mentioned, because ICWNs attempted to perform their roles but did not always have sufficient co-operation from other staff.

TDF 4: Beliefs about capabilities

The beliefs about capabilities domain covered self-confidence, perceived competence, self-efficacy, perceived behavioural control, beliefs, self-esteem, empowerment, and professional confidence.

From the questionnaire, there was high agreement that the "beliefs about capabilities" domain (4.66, 95% CI 4.63 to 4.69) had an impact on hand hygiene behaviour. However, evidence of misunderstanding about hand hygiene practice was found in the focus group, where the belief was expressed that hand hygiene practice are only hand washing with water and soap.

Perceived behavioural control was reported, and the view was expressed that HCWs were likely to perform hand hygiene with more concentration, when caring for a patient in a dirty activity. This was found in almost all the group discussions. Some groups of HCWs also showed less confidence in their ability to perform hand hygiene practice.

Some interviewees expressed doubts about the capabilities of hand hygiene to reduce HCAI, pointing to a lack of evidence in their hospital setting. It was suggested that other aspects of infection control programme might be more effective to reduce HCAI than improving hand hygiene. Some interviewees mentioned the quality of water and towels as limiting their capabilities, and stated that the quality of water and towels needed to be assured before improving hand hygiene.

TDF 5: Optimism

The optimism domain included optimism, pessimism, unrealistic optimism, and identity.

Optimism was expressed in both the focus groups and the interviews that proper hand hygiene by HCWs could prevent HCAIs. There was pessimism that the hand hygiene compliance could be increased to 100 %, because of perceived difficulties in promoting hand hygiene in the hospital.

TDF 6: Beliefs about consequences

The "beliefs about consequences" domain covered beliefs, outcome expectancies, characteristics of outcome expectancies (physical, social, emotional), anticipated regret, and consequents.

From the questionnaire, there was high agreement that "beliefs about consequences" domain (4.46, 95% CI 4.41 to 4.51) had an impact on hand hygiene behaviour. A common outcome expectancy that was found in both the interview and the focus group discussions was that hand hygiene can effectively protect HCWs and patients from infections. Beliefs were also expressed that hand hygiene could result from a feeling of dirty hands.

TDF 7: Reinforcement

The reinforcement domain covered rewards (proximal/distal, valued/not valued, probable/improbable) incentives, punishment, consequents, reinforcement, contingencies, and sanctions.

Rewards from competition were proposed as a potential reinforcement to promote hand hygiene from the focus group. This domain was, however, relatively poorly addressed from both the interviews and the focus groups.

TDF 8: Intentions

The domain "Intentions" covered stability of intentions, stages of change model, and transtheoretical model and stages of change.

From the questionnaire, there was high agreement that the "intentions" domain (4.86, 95% CI 4.84 to 4.88) had an impact on hand hygiene behaviour, but lack of stability of intentions to complete all steps of hand hygiene was found in all groups of focus group discussion and it was suggested that this might be a result of time pressure.

TDF 9: Goals

The "goals" domain covered goals (distal/proximal), goal priority, goal/target setting, goals (autonomous/controlled), action planning, and implementation intention.

From the questionnaire, there was high agreement that the "goals" domain (4.74, 95% CI 4.71 to 4.76) had an impact on hand hygiene behaviour, while goal priority and goal/target setting were important themes in the semi-structured interview from key administrators, and in the focus group of

ICWNs. New staff or new students were considered to be high priority who must receive training on hand hygiene guidelines before starting work.

TDF 10: Memory, attention and decision processes

The "memory, attention and decision processes" domain covered memory, attention, attention control, decision making, and cognitive overload/tiredness.

From the questionnaire, there was high agreement that the "memory, attention and decision processes" domain (4.55, 95% CI 4.52 to 4.59) had an impact on hand hygiene behaviour, while the focus group of ICWNs and nurse aides suggested lack of awareness of correct hand hygiene practice had a negative impact on decision making.

Posters acted as important reminders and were an important determinant of attention control for hand hygiene behaviour of HCWs. Some HCWs stated that when HCW faced rushed periods of work alcohol handrub (AHR) was the preferable decision for hand hygiene practice (and no awareness of the better antibacterial performance of AHR compared to soap and water was demonstrated).

TDF 11: Environmental context and resources

The "environmental context and resources" domain covered environmental stressors, resources/material resources (availability and management), organization culture/climate, salient events/critical incidents, person x environmental interaction, and barriers and facilitators.

From the questionnaire, there was high agreement that the "environmental context and resources" domain (4.75, 95% CI 4.73 to 4.78) had an impact on hand hygiene behaviour. Similar findings were obtained from the focus group discussions.

Lack of resources for hand hygiene in the ward level were addressed in all focus groups as barriers for hand hygiene behaviour, but some interviewees said that proper supplies and resources were available, and they suggested that the reasons behind poor hand hygiene compliance in each ward were more due to failure of resource management instead. A theme expressed by administrators was that quality of resources was questionable because re-useable towels were currently used in this hospital.

TDF 12: Social influences

The “social influences” domain covered social pressure, social norms (subjective, descriptive, injunctive norms), group conformity, social comparisons, group norms, social support (personal/professional/organizational, intra/interpersonal, society/community), power (hierarchy), intergroup conflict, alienation, group identity, and modelling.

From the questionnaire, there was moderately high agreement that the “social influences” domain (3.86, 95% CI 3.81 to 3.90) had an impact on hand hygiene behaviour.

In the focus group discussion, comparison of hand hygiene behaviour among groups of HCWs was reported, and some HCWs claimed that the reasons for their own non-compliance were the non-compliance of other staff as well. Social pressure such as hospital accreditation was thought to be effective in promoting hand hygiene hospital-wide. Physicians were widely considered as role models for hand hygiene behaviour.

TDF 13: Emotion

The “emotion” domain covered fear, anxiety, affect, stress, depression, positive/negative affect, and burn-out.

From the questionnaire, there was high agreement that the “emotion” domain (4.27, 95% CI 4.23 to 4.32) had an impact on hand hygiene behaviour. Fears of carriage of pathogens that can be transmitted to their family were addressed in the focus group, and the view was expressed that this could result in more concentration on hand hygiene by HCWs before going home.

TDF 14: Behaviour regulation

The "behaviour regulation" domain covered self-monitoring, habit-breaking, and action planning.

From the questionnaire, there was moderately high agreement that the "emotion" domain (3.83, 95% CI 3.78 to 3.88) had an impact on hand hygiene behaviour.

From the focus group of nurse aides, in each ward, hand hygiene amongst ward staff was periodically officially monitored by the ICWN. But unofficial monitoring was performed more frequently, and then verbal feedback was immediately provided by the ICWN and considered to contribute to breaking the habit of non-compliance with hand hygiene of the targeted HCW. Lack of knowledge on steps of hand hygiene was also addressed by this form of monitoring.

Interrelations between the relevant domains

By applying the TDF, this section summarises the domain findings by considering the interrelations of the relevant domains from the all relevant domain findings. This section consists of two parts: i) the interrelations of the relevant domains and current knowledge, ii) the interrelations of the relevant domains and current hand hygiene practice.

The interrelations of the relevant domains and current knowledge

For the 1,582 HCWs who completed the questionnaire survey, Pearson's correlation coefficient was used assessing interrelations between survey answers. Interrelations between current knowledge and the relevant domains were considered as having a low association with values of r ranging from - 0.04 to 0.18. No correlation between the knowledge score about hand hygiene from the questionnaire assessment and the belief or "knowledge" domain was seen (r = 0.01). (Appendix C.10)

The interrelations of the relevant domains and current hand hygiene practices

Of 364 HCWs whose hand hygiene practices were directly observed, interrelations between the relevant domains and current hand hygiene behaviour were all found to have only low-level associations with r ranging from -0.07 to 0.16. (Appendix C.11)

4.3.7 Mapping domain finding to the Behaviour Change Wheel's COM-B system

This section links the domain finding to addresses the factors influencing the hand hygiene behaviour by using the COM-B system (Table 4.2) and the model for illustrating individual, team, and organizational levels. (Table 4.3)

Linking the domain findings to the COM-B system

Factor analysis was employed to relate the domain findings to the COM-B system with the aim of identifying factors likely to be important in changing behaviour. Factor analysis of twelve domains yielded a three-factor solution, with a combined explained variation of 100 % (Table 4.9). In considering the factors labels, we linked to the work of the Behaviour Change Wheel's COM-B system, which conceptualized three factors necessary for behaviour to occur[37] (Table 4.3).

The factors were thus labeled as follows: motivation (46.3% of variance, $\alpha = 0.32$), capability (34.5% of variance, $\alpha = 0.00$), and opportunity (19.2% of variance, $\alpha = 0.22$) (Table 4.7 and Figure 4.2).

Capability represented psychological and physical factors that consisted of four domains: knowledge; skills; memory, attention and decision processes; and behavioural regulation. The relevant domains were found to have a low to moderate relation to capability on hand hygiene behaviour, with r ranging from -0.06 t0 0.54.

Opportunity, social and physical factors consisted of two domains: social influences, and environmental context and resources. The relevant domains showed a low to moderate relationship to opportunity for hand hygiene behaviour, with r ranging from 0.05 t0 0.57.

Motivation represented reflective and automatic factors and consisted of six domains: social/professional role and identity; beliefs about capabilities; beliefs about consequences;

intentions; goals; and emotion. The relevant domains were moderately related to motivation on hand hygiene behaviour, with *r* ranging from - 0.06 to 0.64.

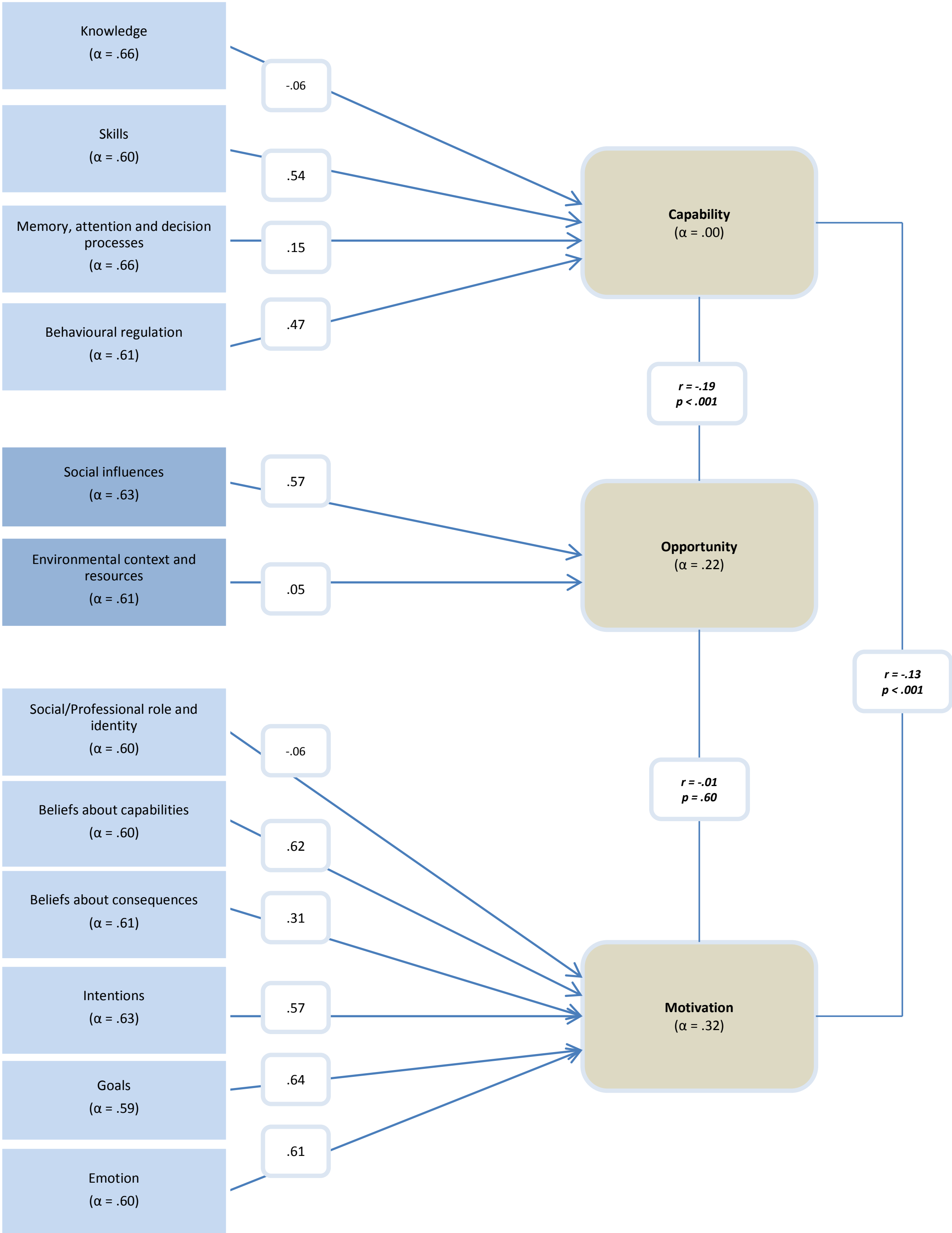
Capability was negatively correlated with opportunity ($r=-0.19, p<0.001$). Capability was negatively correlated with motivation ($r=-0.13, p<0.001$). Motivation was negatively correlated with opportunity ($r=-0.01, p=0.60$).

Table 4.9: Rotated component matrix of theoretical domains and explained variance of each factor for all participants who completing the questionnaire (N = 1,582)

DOMAINS	**FACTORS**		
	Motivation	**Capability**	**Opportunity**
Knowledge	0.28	-0.06	0.05
Skills	0.07	0.54	0.19
Social/professional role and identity	-0.06	0.17	0.58
Beliefs about capabilities	0.62	0.13	-0.004
Beliefs about consequences	0.31	0.50	0.13
Intentions	0.57	0.20	0.09
Goals	0.64	0.18	0.05
Memory, attention and decision processes	0.48	0.15	0.18
Environmental context and resources	0.06	0.72	0.05
Social influences	0.22	0.19	0.57
Emotion	0.61	0.14	-0.06
Behavioural regulation	0.14	0.47	0.25
PERCENT OF VARIANCE	46.3	34.5	19.2

Rotation method: Varimax with Kaiser normalisation

Figure 4.2: Factors and theoretical domains with Cronbach's alpha (α) and domain loading (N = 1,694) Factor correlation (*r*) is provided with p values (two-tailed).



Linking the domain finding to the model for illustrating individual, team, and organizational levels

The level of the constructs in the theoretical domain was illustrated in individual, team, and organizational levels of hand hygiene behaviour based on construct allocations reported by Michie *et al*. [16]

Individual level of hand hygiene behaviour

Environmental stressors including high workload and understaffing were found in this study that affected hand hygiene behaviour of HCWs. Social pressure such as hospital accreditation was addressed in the focus group and was felt to have an impact on individual hand hygiene behaviour hospital-wide.

Team level of hand hygiene behaviour

Social comparison was proposed as a strategy to promote hand hygiene, and was addressed in the focus group discussion with the nurse aides. For example, it was suggested to have a competition on hand hygiene between the wards with each ward designing a strategy to promote hand hygiene on their own ward. The hospital administrator should support the incentives or awards for the winning wards.

Organisational level of hand hygiene behaviour

Resources/ material resources were mentioned and both their availability and their management were discussed. For the availability, lack of hand hygiene supplies were addressed in all sources of data, and the management of the resources was addressed in the interviews of key administrator that needed to improve the management of the resource in the ward level. The quality of resources such as water, towels, was also mentioned and the need for quality-assurance was considered.

4.4 Discussion

4.4.1 Key findings

This study represents one of the first reports applying a theoretical domain framework to identify systematically the barriers or enablers that may affect hand hygiene behaviour of HCWs in resource limited setting. The results showed clear differences across theoretical domains at the individual level, thus suggesting some explanations for implementation difficulties. Fourteen domains of TDF were identified as potential barriers/enablers to hand hygiene practice of HCWs. The domain findings of this study can be considered as determinants of behaviour change.

4.4.2 Comparing study results with other studies

These results are consistent with findings from a systematic review of hand hygiene improvement strategies using a behavioural approach in another setting.[100] From this review, most studies used determinants at the individual and institutional level that corresponded to twelve domains having an impact on behaviour.[100] The findings in this study also show consistency with the questionnaire survey on identifying barriers and levers for best hand hygiene practice of Dyson *et al.* [174] From previous studies[98, 100, 174] the domains of "optimism" and "reinforcement "are less frequently reported to influence hand hygiene behaviour amongst HCWs. Reinforcement using reward incentives has also been reported to have a high association with the successful promotion of hand hygiene in the review and network meta-analysis of the comparative efficacy of interventions to promote hand hygiene by Luangasanatip *et al.*[82]

The current study aimed to address both barriers and enablers as determinants for different levels of behaviour. Because HCWs in the hospital usually work as teams the relations between HCWs and their impact on hand hygiene behaviour needs to be understood before designing the intervention. Strategies to improve hand hygiene could include focus at the individual level, involving consideration of intrapersonal factors, and the consideration of the institutional level (such as ward level or hospital level, where the local context of each ward/hospital could be considered in the development of an intervention), which involves interpersonal and community factors. [21]

The studies by Fuller *et al.*[108] and Gould *et al.*[175]conducted interventions to promote hand hygiene by engaging the ward in the process of implementation. Consistent with findings of this study that correlation between social context and individual factors on hand hygiene behaviour are addressed in groups of hand hygiene observations (individual interactions within group: verbal reminding in the ward) and in the focus group, such as routine monitoring of ICWNs acting either as an official or unofficial monitor affected individual behaviour. These finding echo results from previous intervention studies on health behaviour that the domain social influence is considered relevant to successfully change behaviour.[176]

Knowledge of hand hygiene is frequently reported as one of the most important determinants that affect hand hygiene behaviour.[100, 177, 178] In this study, lack of knowledge of HCWs was strongly suggested in the focus groups and in the direct observations, and ignorance about the greater antibacterial properties of alcohol handrub compared with soap and water appeared to be widespread. Conversely, in the semi-structured interviews with key administrators and in the knowledge scores from self-administrated questionnaire the view was expressed that knowledge about hand hygiene was sufficient. All HCW beliefs on “knowledge” domain were also are reported as having a big effect on hand hygiene behaviour, but skeptism about the value of the hand hygiene to prevent HCAI was revealed by all methods. Self-reported hand hygiene behaviour is usually considered as over-reporting: this has been found in this study and in several previous studies as well.[179-181] In this study, self-reported hand hygiene compliance was found to be 10 times higher than that recorded by direct observation.

4.4.3 Theoretical implications

There are implications here for theories of behaviour change as applied to hand hygiene. We can more precisely define barriers and enablers on hand hygiene behaviour and their relevance for implementation of interventions in other resource-limited setting using this approach. This method may also be used to get a systematic understanding of other health professional behaviour in other resource-limited settings as well. It can help to identify target groups and whether changes in the domains are likely to directly influence implementation of intervention. The Behaviour change Technique (BCT) Taxonomy (v1) has been developed to standardize the reporting of intervention content, and identify their potentially 'active ingredients'.[182]

4.4.4 Practical implications

Intervention development should include identifying relevant domains as a key part of the process.[94, 95] Recently health professional behaviour in a range of clinical areas has been investigated by using the TDF. Relevant domains were identified in the processes of intervention development.

In linking theoretical domains to BCTs, BCTs provide a guide for how to do this.[183] Each technique may work best if it is designed for and adapted to the individual context. When designing interventions to improve hand hygiene, target domains should not only be selected but also the relevance of each domain to behaviour change should be considered as well.

Example of using the BCT Taxonomy[176] to guide intervention development on the basis of TDF analyses are seen in antibiotic prescribing[184] and hand hygiene.[99, 185] Characterisation of implementation of interventions in terms of behaviour change techniques and theory has been reviewed by Steinmo *et al.* [186] This has helped to illustrate the utility of the Behaviour Change Wheel (BCW), the BCT Taxonomy and the TDF, tools recognised for providing guidance for intervention design, and for characterising an existing intervention to implement evidence-based care.[186]

4.4.5 Strengths, limitations and future directions

A key strength of this study is using triangulation to identify the factors associated with hand hygiene from different viewpoints. For example, comparing direct observation on hand hygiene with self-reporting of hand hygiene practice, and using qualitative and quantitative approaches. A second strength is applying a systematic approach to explore the factors affecting hand hygiene behaviour, which can be linked to behaviour change techniques in the intervention phase as well.

There are some limitations in this study. First, the allocation of certain items to domains was not always clear. Second, some domains might have overlapping meaning in study settings that can affect the study results such as the domain social/professional role and identity and the domain social influences. Third, a small number of questions for each domain may affect the reliability of the results. Excluding the domain optimism and reinforcement from the belief survey may have had some effect on the results of the factor analysis.

Future research is needed to evaluate how these domains relate to behaviours targeted in the promotion of hand hygiene, and how various interventions can change these behaviours.

4.5 Conclusions

This study has demonstrated a feasible method to identify the potential barriers/enablers to hand hygiene practice of HCWs using a TDF approach, highlighting factors that need to be addressed before designing interventions. Understanding hand hygiene behaviour among HCWs is important part of changing behaviour. The results are of potential use for designing interventions to promote hand hygiene.

Chapter 5

Impact of a multimodal hand hygiene improvement intervention

5.1 Introduction

Healthcare-associated infections (HCAIs) are a global problem and a major source of preventable morbidity and mortality worldwide, but particularly so in low and middle income countries (LMICs).[4] A recent review estimated the pooled prevalence of HCAI in developing countries (defined as Organization Economic Co-operation Development (OECD) low or middle income countries) to be 15.5 per 100 patients, and highlighted the need to improve infection control practices.[4] Rates of surgical site infection have been reported to range from 12 to 39% in developing countries compared to 2 to 5% in developed countries and rates of HCAI in neonates have been found to be 12 times higher in developing countries.[5, 6] Mortality due to such infections in developing countries is found to greatly exceed that in developed countries.[7]

There is, however, evidence from quasi experimental research that concerted and sometimes low-cost interventions are able to greatly reduce the hospital transmission and prevalence of multi-drug resistant organisms (MDROs),[187] resulting in improved patient outcomes.[17]

Improving hand hygiene practice among healthcare workers (HCW), in particular, is thought to substantially reduce the transmission of important healthcare-associated pathogens resulting in reduced incidence of healthcare-associated infection (HCAI).[17, 79, 158, 188-190] Such interventions are relatively inexpensive and thought likely to be cost-effective (and potentially cost-saving as a result of reduced infections rates).[191]

However, a 2010 Cochrane review has highlighted the lack of methodologically sound research evaluating interventions to improve hand hygiene: only four studies met the minimum inclusion criteria and no study came from a lower- or middle-income country.[7] An increasing number of "high quality" studies on interventions for hand hygiene after 2009 have been reported in the latest systematic review in 2015; using the same criteria as in the previous review 41 studies met the inclusion criteria, and also 5 of these came from a lower- or middle-income country.[82]

Moreover, an earlier review identified a need for stronger study designs to link improved hand hygiene compliance with reductions in HCAIs (currently such evidence is based only on observational studies).[7] There are also very few evaluations of such intervention using strong study designs in lower and middle income countries (LMICs).[47, 82]

Previous data from our research setting has suggested hospital infection control guidelines may not have been implemented consistently due, in part, to resource constraints.[14] More recent qualitative research carried out at our hospital site into the causes of poor hand hygiene compliance identified several obstacles to improving appropriate hand hygiene behavior (see chapter 4).

Available evidence suggests that hand hygiene promotion (HHP) with the components of the WHO multimodal hand hygiene improvement strategy is an effective approach to improve HCW hand hygiene compliance.[47, 82] The World Health Organization (WHO) has developed evidence-based "WHO Guidelines on Hand Hygiene in Health Care" to support health-care facilities to improve hand hygiene and thus reduce HCAI.[89] The strategy described in these guidelines has been designed to be used by any health-care facility, irrespective of the level of resources or whether the facility has already implemented any hand hygiene initiatives.

This approach promoted by the WHO guidelines identifies five moments for hand hygiene (before patient contact, before aseptic procedure, after body fluid exposure, after touching a patient, after touching a patient's surroundings).[89] These guidelines aim to encourage good hand hygiene compliance in the real world and recommend a multimodal HHP strategy making use of five components: 1) system change (for example, changing systems to ensure that alcohol-based hand-rub (ABHR) is readily available wherever and whenever needed), 2) training and education, 3) observation and feedback, 4) reminders in the hospital, and 5) a hospital safety climate.[89]

In conclusion, there is a need for methodologically rigorous research to evaluate the impact of a multimodal intervention based on the WHO recommendations. The need for such research is greatest in resource-constrained settings in lower and middle income countries where the burden of disease due to HCAIs is the greatest. Adapting WHO's guidelines to local conditions is important and there is a need to generate action plans which are appropriate to their own setting.

The aim of this study was to evaluate the impact of a multimodal intervention to improve hand hygiene in HCWs on directly observed compliance with the WHO's recommended five moments for hand hygiene in a LMIC setting using a using a cluster-randomized trial.

5.2 Methods

5.2.1 Participants and Setting

The study site was a 1000-bed hospital, which is located in the northeast of Thailand. This hospital provides facilities serving a medical school, residency training, tertiary care, and is a regional referral center for the northeast part of Thailand. For this study we recruited 58 wards including 20 intensive-care-unit wards (ICU wards) and 38 non-intensive-care-unit wards (non-ICU wards).

The total number of admission is around 70,000 per year. This hospital has a specialist infection control team (ICT) including four specialist infection control doctors (ICDs) (2 for children, and 2 for adults), four specialist infection control nurses (ICN), and one assistant. The role of this ICT is very multi-faceted, and involves planning, monitoring, evaluating, updating, and educating. Its function is to prevent and control nosocomial infections.

Our study setting also has an infection control committee (ICC). The ICC includes key administrators from all departments of the hospital. The role of the ICC is similar to the ICT at an administrative level. Each ward has at least one infection control ward nurse (ICWN), who has been specially trained on guidelines for infection control by the ICT and is the responsible person to lead and coordinate with ward staff and the ICT to prevent and control nosocomial infections in their own ward.

Participants were all HCWs, having direct patient contact in at least one of these 58 in-patient wards at the hospital site.

Eligibility Criteria

All HCWs with direct patient contact (physicians, nurses, aides, and ancillary staff) were included in the study. Visitors and hospital staff such as medical students, nursing students, physical therapists, and radiologists were also included. There were no exclusion criteria.

5.2.2 Ethics statements

Ethical permission for this study was obtained from the Ethical and Scientific Review Committees of Faculty of Tropical Medicine, Mahidol University, Thailand, and of hospital site (Appendix D.1). The study protocol and its associated documents were also approved.

5.2.3 Study design

The research design was a prospective stepped wedge trial using a ward as the study cluster. A stepped wedge design is a type of cluster randomized controlled trial which is appropriate when there are prior reasons to believe the intervention will be beneficial (as opposed to equipoise) and when it is impractical to deliver the intervention to all study units simultaneously.[105, 192] Both conditions hold here.[105, 192, 193]

The time step in which the intervention was made in each ward was randomly selected using computer-generated sequences. All of the 58 in-patient wards at the hospital were randomly selected (using a computer generated sequence) to assign the order of applying the intervention at each time step.

5.2.4 Study Duration

The study duration was 74 weeks between 1st December 2013 and 2nd May 2015. The study was divided into 3 phases;

1) The pre-intervention period was planned as a 5-week baseline period and was actually conducted between 1st December 2013 and 4th January 2014 (a total of 5 weeks).
2) The intervention period was planned to last 58 weeks but was actually conducted between 5th January 2014 and 28th March 2015 and lasted a total of 64 weeks.
3) The post-intervention period was planned as a 5-week follow-up period, and was actually conducted between 29th March and 2nd May 2015 (a total of 5 weeks).

5.2.5 Study intervention

The WHO Multimodal Hand Hygiene Improvement Strategy [46] was applied as the study intervention, making use of five components as described in section one (Table 5.1) with the aim of inducing behavioural change in relation to improved hand hygiene.

The intervention aimed to engage participating ward staff in the decision-making process of how to apply the WHO multimodal strategy to their ward. This engagement made use of a “Menu” provided to ward staff to help them design a customized intervention for their ward. The Menu contained four key elements. The first was the detail of each component of the WHO strategy with a number of suggestions for how this could be applied and a minimum requirement for implementing each component. The second was detail of the stepwise approach, which determined the intervention steps. The third contained detail of the WHO recommendations for implementation of each component of the WHO strategy. The last was the ward assessment that allowed the ward to consider all components of the strategy, and how each component could best be implemented in that particular ward and to provide the reasons why specific intervention components should or should not be applied (Appendix D.2).

The ward could freely decide to adapt the sequence of implementing the five components but they were asked to come up with a definite plan for implementing all components. A blank sheet for the original ideas of the ward to generate improvement strategy components that did not necessarily fit into WHO-defined five components was also provided under supervision of the ICT and research team.

A “Guide to the Implementation of the WHO Multimodal Hand Hygiene Improvement Strategy”[46] was translated in Thai as the intervention manual. This was made available to all wards in two forms: an electronic file and a hard copy.

Table 5.1: Description of the key components of the intervention

The intervention components	Definition/Activity
System change [a]	Ensuring that the necessary infrastructure/materials are in place to allow health-care workers to practice hand hygiene. This includes two essential elements: • access to a safe, continuous water supply as well as to soap and towels; • readily accessible alcohol-based handrub at the point of care. [b]
Training / Education [a]	Providing regular training on the importance of hand hygiene, based on the “My 5 Moments for Hand Hygiene” approach, and the correct procedures for handrubbing and handwashing, to all health-care workers.
Evaluation and feedback [a]	Monitoring hand hygiene practices and infrastructure, along with related perceptions and knowledge among health-care workers, while providing performance and results feedback to staff.
Reminders in the workplace [a]	Prompting and reminding health-care workers about the importance of hand hygiene and about the appropriate indications and procedures for performing it.

[a] Adapted from the WHO multimodal hand hygiene improvement strategy (http://www.who.int/gpsc/5may/Guide_to_Implementation.pdf) [46]

[b] Point of care – The place where the patient, the health-care worker, and care or treatment involving contact with the patient or his/her surroundings occurs.

Table 5.1: Description of the key components of the strategy on the intervention (cont.)

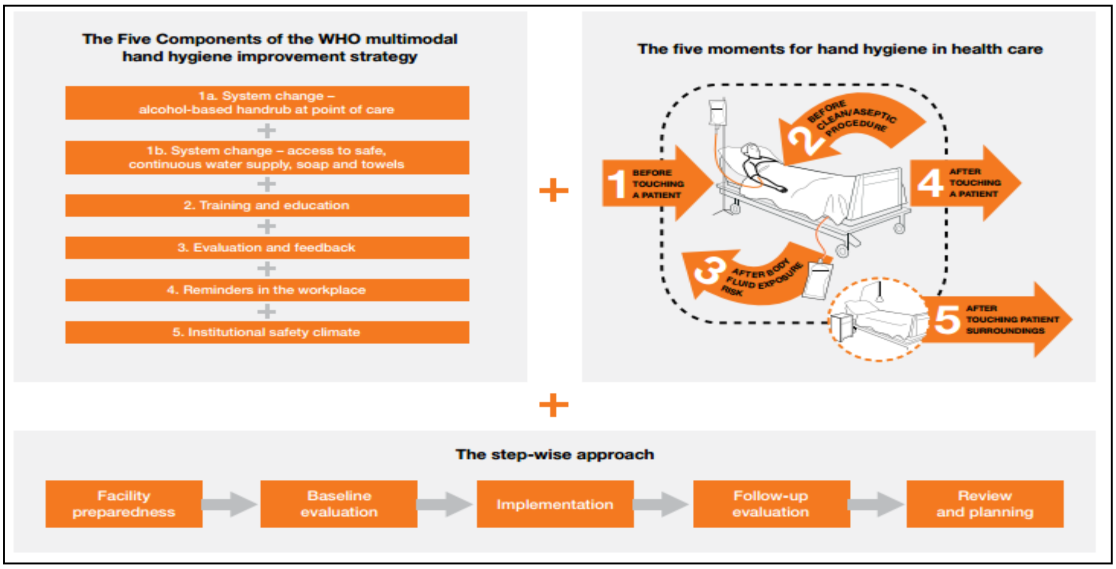
The intervention components	Definition/Activity
Institutional safety climate [a]	Creating an environment and the perceptions that facilitate awareness-raising about patient safety issues while guaranteeing consideration of hand hygiene improvement as a high priority at all levels, including • active participation at both the institutional and individual levels; • awareness of individual and institutional capacity to change and improve (self-efficacy); and • partnership with patients and patient organisations.
An initiative idea	In addition to being asked to select the best way to implement the five components above on their own ward, each ward was encouraged to generate their own action plan for promoting hand hygiene on their own ward, possibly using measures that did not fit into any of the above five components.

[a] Adapted from the WHO multimodal hand hygiene improvement strategy (http://www.who.int/gpsc/5may/Guide_to_Implementation.pdf) [46]

[b] Point of care – The place where the patient, the health-care worker, and care or treatment involving contact with the patient or his/her surroundings occurs.

The step-wise approach of the WHO Multimodal Hand Hygiene Improvement Strategy [46] was applied as part of the implementation process. This included 5 steps: step 1, facility preparedness – readiness for action; step 2, baseline evaluation – establishing knowledge of the current situation; step 3, implementation – introducing the improvement activities; step 4, follow-up evaluation – evaluating the implementation impact, and step 5, the ongoing planning and review cycle (Figure 5.1).

Figure 5.1: Implementation process summary: the WHO multimodal hand hygiene improvement strategy, the "My 5 Moments for Hand Hygiene" approach, and the step-wise approach. (from: http://www.who.int/gpsc/5may/Guide_to_Implementation.pdf) [46]



5.2.6 Study procedures

Before starting this study:

Hand hygiene is considered as general and essential part of infection control practices.[73] Hand hygiene intervention programmes are one part of the regular work for infection control teams (ICTs) in Thailand,[69] and the hospital infection control departments were familiar with such interventions. [69]

However, despite prior interventions, the study hospital had not been successful in attaining acceptable hand hygiene levels.[69, 71, 86] It was anticipated that by actively engaging ward staff in designing their own interventions within the framework of the WHO multimodal strategy the limitations of previous interventions could be overcome. In this study the aim was, therefore, to work together with the hospital in implementing an intervention to improve hand hygiene compliance in HCWs and not intervene in their routine hospital work or require use of resources not usually available to them (since the aim was to develop a generalizable intervention that could be applied to other hospitals in LMICs).

Before starting this study, an overview of the study was given to the ICT and hospital director and their permission requested to perform the study including direct observation of hygiene practices for all HCWs. The meeting day for opening of the study by the hospital's director was 8th January 2013. At this meeting overall details of the study were given to the head nurses of all the study wards.

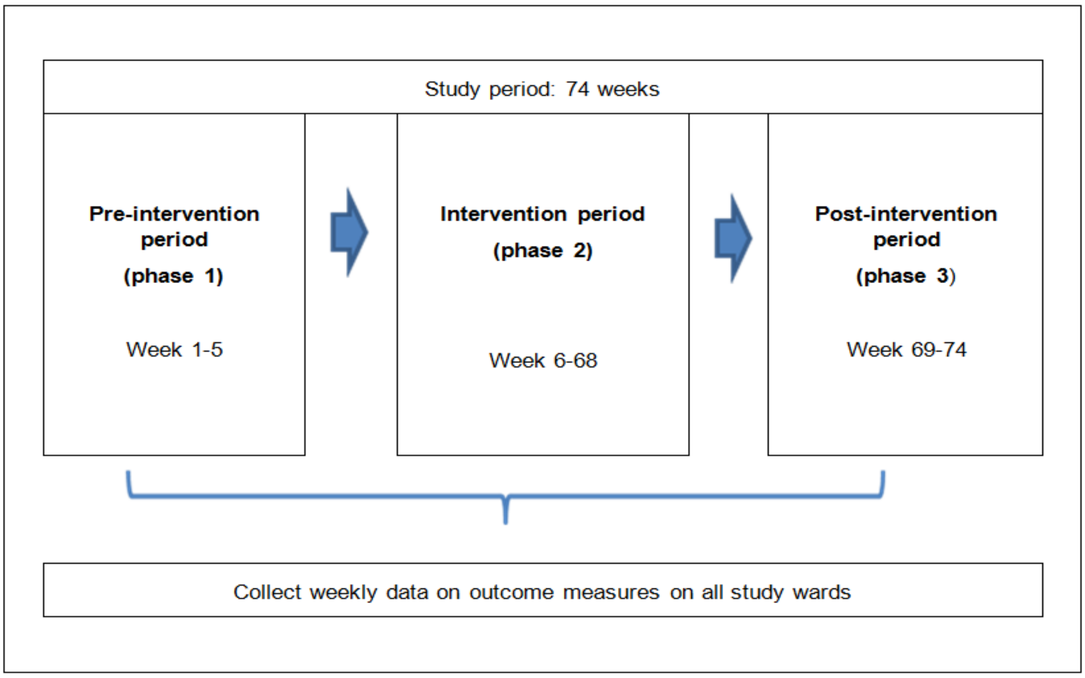
During this study:

This study was divided into 3 phases (Figure 5.2):

- Pre-intervention period: A 5-week baseline period where outcome data were recorded from all wards but no interventions were made.
- Intervention period: A 64-week intervention period during which the intervention was applied to each ward in turn.

- Post-intervention period: A 5-week follow-up period, where no further interventions were made but during which outcome data continued to be recorded

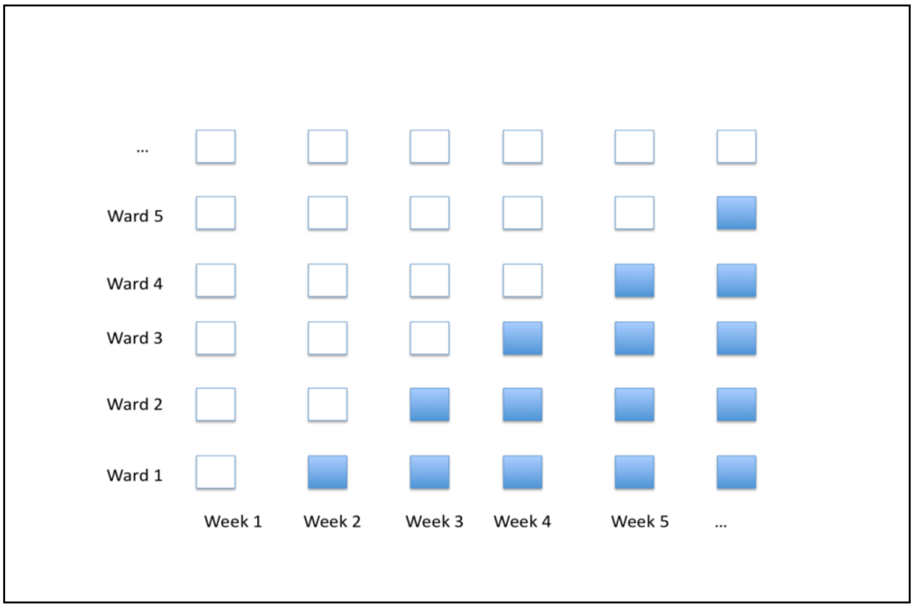
Figure 5.2: Study phases



Implementation of the intervention

After the pre-intervention phase, the wards were randomized into the intervention step at one month intervals (Figure 5.3). The intervention was initially applied to one new randomly-selected ward each week during the intervention period. The order in which wards received the intervention was selected randomly using a computer generated randomization scheme.

Figure 5.3: Stepped wedge design of phase 2 of the hand hygiene intervention. Shaded cells represent intervention periods. All wards receive the intervention, but the ward receiving the intervention in a given week is selected randomly from those wards that have not yet received the intervention. Once wards have received the intervention they remain in the intervention arm.



One month prior to the intervention date for each ward they were notified by the research team and ICT (the ICT were responsible for delivering the intervention) requesting an appointment between the ICT and each ward to facilitate them designing an intervention plan to address the five components of the WHO intervention and to make plans to provide the training and other aspects of the intervention to ward staff. A new ward was selected at random for the intervention if the selected wad was currently closed (or expected to be closed at the intervention date). The notification included a summary of intervention details and procedures in two pages. All appointments took place as person-to-person meetings and appointments were arranged by phone calls to the wards. These meetings were also used to clarify the study information and requirements.

If the staff on the selected ward were unwilling or unable to receive the intervention on the specified date, then the randomly selected intervention week was still used for the intention to intervene analysis but the research team and ICT found an alternative date for the meeting with the ward staff. The window period for the intervention was considered to last from the start of the randomly selected intervention date until one month after this date. However, in case of delays in delivering the intervention the research team and ICT was also asked to record the date when the intervention was actually provided to the selected ward, and this date was used for a secondary per protocol analysis.

Intervention procedure:

- *One month before intervention date:* communication with randomized ward approximately one month before the intervention during the monthly meeting of head nurses (which occurs on the 20^{th} of each month). This aimed to get three available days of infection control ward nurse (ICWN) or representative staff, who received the intervention in each ward intervention.
- *Day 1 of intervention week:* representatives of each ward were asked to present the current infection control practice and current situation with respect to hand hygiene practice of the ward to the head nurse and study team. This meeting should have included ICD, ICN, and research team and lasted around 30 minute. Then the study team explained the intervention menu and gave ward staff the intervention materials including the component menu and the Thai language translation of the manual "A Guide to the Implementation of the WHO Multimodal Hand Hygiene Improvement Strategy".
- *Day 2 of intervention week:* the ICWN of each ward was coached and supported in making an action plan specific to their ward for promoting hand hygiene on their ward addressing the five components of the WHO strategy. The study team was also present at this meeting which lasted around 30 minutes. The ward staff members present at this meeting freely

decided to select which components in the intervention menu to implement taking into account the local circumstances in their ward and the overall need to address all five components of the WHO strategy.

- *Day 3 of intervention week:* the new plan of hand hygiene practice developed by ward staff was presented by the ICWN of the intervention ward to the head nurse and study team. This lasted around 30 minutes.
- *Within a month of intervention:* the implementing ward was required to set a meeting to explain the action plan to all ward staff, and each ward was asked to summarize the meeting and send a report to the ICT.
- *Every month after intention week:* implemented wards were asked to hold a meeting to re-assess the action plan with all staff and, if necessary, revise plans to promote hand hygiene under the supervision of the ICT.

Fidelity to intervention

Fidelity to intervention may be defined as the extent to which delivery of an intervention adheres to the origin protocol. The total number of the meeting reports that were returned to the ICT for updating action plans of the implemented intervention were considered as a measure of the fidelity to intervention.

Fidelity to intervention was also assessed by both direct ward-based observations by the research team and through interviews with the ICT. The ward-based observations of all study wards were performed by observers every week and allowed assessments of reminders in the work place and evidence of system change (for example, by assessing whether systems were in place to ensure alcohol handrub bottles were not empty, and soap and towels were available at sinks, or other facilities at point of care).

The ICT interviews were intended to be conducted with ward staff in all wards receiving the intervention one month after the intervention. These interviews also aimed to ensure that the intervention was acceptable to staff and did not result in any unanticipated adverse consequences either for staff or patients.

5.2.7 Data Collection

Directly observed hand hygiene compliance data were collected during all three phases of the study by observers. Each observed session was performed in each ward in each week of the study. This required at least 58 observed sessions in this 58-ward study in each study week. Data on hand hygiene compliance from a minimum of five opportunities were collected from each ward during each week of the study.

As hand hygiene promotion was the current practice of infection control nurses and was standard practice throughout hospital site, this study aimed to assess the practice of hand hygiene without informing the participants that they are being watched. This was to reduce potential bias as previous studies provide strong evidence that HCWs will change their behavior if they know that they are being watched and that changed behavior is temporary and does not reflect the real practice (a Hawthorne effect).[102, 194]

Three months prior to staring the study, the observers were trained in observation methods to record hand hygiene compliance data. Observation methods were in accordance with WHO recommendations, using tools for training and education for observers provided by the WHO (http://www.who.int/gpsc/5may/tools/training_education/en/) and also making use of the WHO's "5-movements" framework and the standard WHO hand hygiene compliance observation forms.[47, 102, 195] The "My 5 Moments for Hand Hygiene" approach encourages health-care workers to clean their hands (i) before touching a patient, (ii) before clean/aseptic procedures, (iii) after body fluid exposure/risk, (iv) after touching a patient and (v) after touching patient surroundings. Hand hygiene observation data were entered daily on the secure password-protected study database, which was implemented in OpenClinica®.

5.2.8 Outcome measurements

The primary outcome was directly observed compliance with the WHO's recommended five moments for hand hygiene amongst HCWs having direct patient contact. The compliance comparison was between pre-intervention and post-intervention rates of directly observed hand hygiene compliance within wards.

The trained observers collected the outcome data. Reliability among observers was assessed during the study to determine whether there was consistency in data collection between observers. Reliability among observers is often referred to as inter-observer reliability (inter-rater reliability). After two or more observers observe and document the same event, inter-rater reliability was determined by comparing the amount of agreement or disagreement in their assessments or measurements. Cohen's kappa statistic was used to record inter-rater reliability between the observers. [170] Cohen suggested the Kappa result be interpreted as follows: values ≤ 0 as indicating no agreement and 0.01–0.20 as none to slight, 0.21–0.40 as fair, 0.41– 0.60 as moderate, 0.61–0.80 as substantial, and 0.81–1.00 as almost perfect agreement.[170]

5.2.9 Statistical considerations

Sample size calculation

Power calculations were performed using equations 7 and 8 from Hussey & Hughes (2007).[104, 106] Assuming 58 wards, and 60 one week time periods with the observation of at least of five of hand hygiene opportunities per ward per week throughout the study, the power to detect increases in hand hygiene compliance significant at the 5% level are given in Table 5.2 below.

These calculations assume extra binomial variation in hygiene compliance increases the outcome variance by a factor of two (such extra binomial variation could occur if staff are more likely to comply with hand hygiene guidelines if they see other staff complying with guidelines in the same period). Accounting for such extra binomial variation is conservative as it will decrease the power compared with the corresponding approach without such extra binomial variation.

These results show that the study had good power (>90%) to detect 2% increases in hand hygiene compliance if initial hand hygiene compliance was very low (~5%), and very high power to detect increases of 5% or more under all scenarios. They also confirm the observation that power in stepped wedge designs tends to be relatively insensitive to the intra cluster correlation coefficient (in contrast to parallel cluster randomized controlled trials).[104, 106]

Table 5.2: Power to detect increases in hand hygiene of compliance of 2 or 5% significant at the 5% level as a function of baseline hand hygiene compliance and the intra cluster correlation coefficient

Baseline hand hygiene compliance	Increase in compliance after intervention	Intra cluster correlation coefficient				
		0.01	0.05	0.1	0.2	0.5
5%	2%	93%	91%	91%	91%	91%
5%	5%	100%	100%	100%	100%	100%
10%	2%	70%	67%	67%	66%	66%
10%	5%	100%	100%	100%	100%	100%
15%	2%	55%	52%	52%	52%	52%
15%	5%	100%	100%	100%	100%	100%
20%	2%	46%	44%	43%	43%	43%
20%	5%	100%	99%	99%	99%	99%
30%	2%	37%	35%	35%	35%	34%
30%	5%	98%	98%	97%	97%	97%

Statistical analysis

The primary analysis was done on a per-protocol basis (using the dates at which each ward was randomized to receive the intervention). Response functions for modelling the effect of the intervention allowed for both changes in level and trend of outcome measures. The analysis was performed at the cluster level, with observations of hand hygiene compliance within each ward for each time period (week of study) and used a multilevel logistic regression model which is a type of generalized linear mixed model (GLMM). A GLMM is an extension to a generalized linear model (GLM) that accounts for random effects (random effects in this case are important for accounting for the fact that outcomes are more likely to be similar within each ward).

Analysis was performed using STATA version 14.0 (StataCorp LP, College station, Texas) and using the *melogit* command to fit a GLMM of the relationship between proportion of the hand hygiene compliance and intervention week. The command of the GLMM is:

melogit sum_overall Rx1 week post_ran i.week || ward:, binomial(sum_opp) or

As fixed effects, the intervention (Rx1 which is 0 in weeks before the intervention and 1 in weeks after the intervention), week, and post-intervention week number (week post_ran) entered into the model. This allowed the model to account for a stepwise changes associated with the intervention as well as pre-intervention and post-intervention trends. The categorical variables (i.week) also adjusted for week number, allowing for possible seasonal effects. In the random effect model, we assume the intercepts for the effect of intervention differ between the wards to account for the cluster effect of the wards (this is represented by "|| ward" in the STATA command). P-values were obtained using likelihood ratio tests comparing the full model with the effect in question against the model without the effect in question.

In the above command sum_overall is the number of total occasions of correctly performing hand hygiene in a particular ward in each week while sum_opp represents the number of opportunities.

The overall compliance for each ward in each week was calculated as the average compliance over all observed hand hygiene opportunities. The calculation of hand hygiene compliance was provided as follows:

$$\text{Compliance (\%)} = \left[\frac{\text{Actual number of opportunities where correct HH was observed}}{\text{Number of the observed HH opportunities during observation}}\right] \text{X } 100$$

Additionally, an intention-to-intervene analysis (using the dates when wards actually received the intervention) was performed using the same multilevel logistic regression analysis accounting for clustering at the ward level. Subgroup analyses were performed for hand hygiene opportunities corresponding to each one of the “five moments”.

5.3 Results

5.3.1 Study flow

The trial start and finish date were specified as 24th December 2013 – 2nd May 2015 (a 74-week period). There were 57 wards included in 57 randomized steps (one step for each ward). The original plan had specified a 58-week intervention phase for implementing intervention, but one ward did not implement the intervention because an appointment to implement the intervention in the intervention phase could not be made.

Thirty-eight wards (65.5%[38/58]c) initiated implementation of the intervention within one month of the time specified at randomization There was a mean delay from the planned time of starting the intervention to the actual time of 1.1 weeks (interquartile range [IQR] 0-3 weeks, range 0-4 weeks).

Nineteen wards (32.8% [19/58]) had a delay in implementing the intervention that was greater than one month with a mean delay in implementation of 24.1 weeks (IQR 9-37 weeks, range 5-56 weeks). To ensure that the last ward had a 5-week period of data collection post-intervention, the data collection was extended for all wards by six weeks to 2nd May 2015.

Reasons for these delays fell into two types: those reflecting hospital-wide factors which affected all wards, and ward specific factors. Hospital-wide factors were i) staff changes (a new head of each ward started on 1st of October of each year, and it was necessary to explain details of the study again to new ward heads); and ii) during hospital accreditation (all wards were requested by ICT to postpone interventions to prepare and perform activities for this accreditation event). Individual reasons included high workload and few staff available during the particular week a ward was randomized to receive the intervention. Figure 5.4 shows a timeline of the different study phases and actual weeks of implementation.

Inter-rater reliability was assessed before and during the study on a monthly basis by asking the observers to record hand hygiene compliance data independently during observation of the same hand hygiene opportunities. A total of 18 times of inter-rater reliability from the observers was assessed throughout the study period with a mean score of 0.928, which was considered as almost perfect agreement.[170] Appendix D.3 shows detail of all assessment of inter-rater reliability.

5.3.2 Number analyzed

For the outcome, intention-to-intervene analysis was performed for the 58 randomized wards into the intervention. An additional per-protocol analysis was also performed for the 57 implementing wards using the actual week of implementing the intervention.

If fidelity to intervention had been 100%, then, in addition to actually implementing interventions addressing each of five components of WHO strategy at the pre-specified time, each ward should have produced a report summarizing the outcome of the ward meeting to generate the action plan for improving hand hygiene practice in their ward for each of five intervention components, and meeting reports after implementing the intervention which should have been returned to ICT every month or every time that they had a meeting. The total number of reports returned was 18, range 0-2 per ward, representing 7.0 % of the 258 reported expected from 57 wards. Data were available from all wards as to whether 0 or 1 report had been returned each month of the study. The assessment of fidelity by the research team found some implementing wards were doing activities to promote hand hygiene without sending any meeting reports to the ICT.

5.3.3 Hand hygiene compliance observations

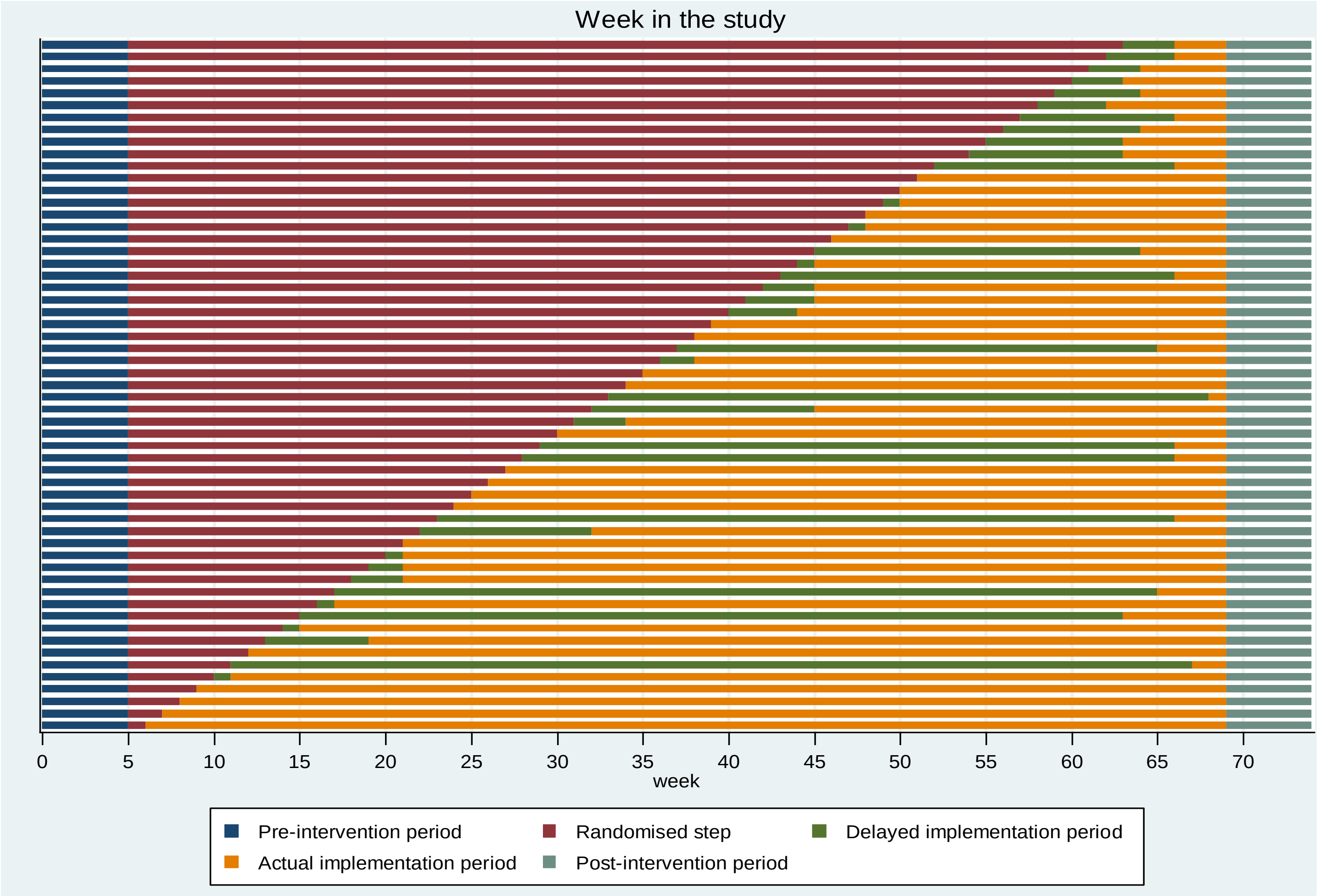
A total of 4,206 hand hygiene observation sessions with a total of 20,709 repeatedly observed HCWs (Appendix D.4) were performed and there were 57,076 observed hand hygiene opportunities from 58 wards (Table 5.3, and Appendix D.5). The mean number of observed HCWs in these observation sessions was 1.1 (IQR 1-1 HCWs, range 1-5), and the mean number of observed opportunities per ward per week was 17.8 (IQR 11-22, range 1-90). A summary of the characteristics of all study wards is presented in Appendix D.6.

During the five pre-intervention weeks, there were 3,994 hand hygiene opportunities observed with an overall hand hygiene compliance rate of 8.89 % (355/3,994) and a ward-level weekly compliance ranging from a low of 0 % to a high of 100 %.

During the 64-week intervention period, 49,792 observations were made. In 5,142 of these hand hygiene compliance was observed (10.33%), and ward-level weekly rates ranged from 0% to 100%.

For the five post-intervention weeks, there were 3,290 observations, with an overall hand hygiene compliance rate of 9.67 %, (318 /3,290) with the ward-level weekly rates ranging from 0% to 100%. Figure 5.5 presents the hand hygiene compliance data for each ward in the study.

Figure 5.4: Timeline of study period for randomization and implementation



Note: Dark blue is pre-intervention period. Dark red is randomized week. Green is period of delayed implementation. Orange is actual implementation period. Grey is post-intervention period.

While overall changes in compliance were small, improvements in hand hygiene compliance were found in 27 wards after implementing the intervention, and in five wards the intervention was associated with a doubling of their pre-intervention compliance rate. Appendix D.7 presents the change in hand hygiene compliance comparing values before and after the intervention for each ward.

More than half of the observed hand hygiene opportunities came from registered nurses (54.96% [31,369/57,076]), followed by nursing aides (19.03% [10,863/57,076]), and hospital support staff, who are responsible to clean around the patient zone (6.85% [3,911/57,076]). While only 20 of 57 wards were ICU wards these accounted for the majority of observed hand hygiene opportunities (67.32% [38,425/57,076]), while one third of observed opportunities (32.67% [18,651/57,076]) came from the 37 non-ICU wards (Table 5.3). Summaries of all observed HCWs by characteristics and covariates in the study are shown in Appendix D.8, while characteristic of HCWs are presented in Table 5.4.

The highest improvement in hand hygiene compliance was for visitors (3.52% before intervention vs. 7.41% of after intervention), followed by physicians (5.41% before intervention vs. 8.21% of after intervention), and nursing aides (4.12% before intervention vs. 6.90% after interventions). The rate of hand hygiene compliance in the department of obstetrics and gynecology nearly doubled (3.07% of before intervention vs. 6.92% of after intervention) (Appendix D.9). Comparisons of hand hygiene compliance by characteristic variables and before and after the intervention are presented in Appendix D.9, Appendix D.10, and Appendix D.11.

Table 5.3: Descriptive opportunity for hand hygiene by characteristics and covariates in the study

Variable	Before intervention n (%)			After intervention n (%)			Overall n (%)		
	Not performed	Performed	Total	Not performed	Performed	Total	Not performed	Performed	Total
Overall	**30,954 (89.9%)**	**3,476 (10.1%)**	**34,430 (100%)**	**20,307 (89.7%)**	**2,339 (10.3%)**	**22,646 (100%)**	**51,261 (89.8%)**	**5,815 (10.2%)**	**57,076 (100%)**
Sex									
Male	7,419 (94.7%)	418 (5.3%)	7,837 (100%)	3,572 (92.2%)	302 (7.8%)	3,874 (100%)	10,991 (93.9%)	720 (6.1%)	11,711 (100%)
Female	23,535 (88.5%)	3,058 (11.5%)	26,593 (100%)	16,735 (89.1%)	2,037 (10.9%)	18,772 (100%)	40,270 (88.8%)	5,095 (11.2%)	45,365 (100%)
Type of HCW									
Doctor	1,730 (94.6%)	99 (5.4%)	1,829 (100%)	559 (91.8%)	50 (8.2%)	609 (100%)	2,289 (93.9%)	149 (6.1%)	2,438 (100%)
Registered Nurse	15,979 (85.4%)	2,723 (14.6%)	18,702 100%)	11,003 (86.9%)	1,664 (13.1%)	12,667 (100%)	26,982 (86.0%)	4,387 (14.0%)	31,369 (100%)
Technical Nurse	515 (87.6%)	73 (12.4%)	588 (100%)	446 (88.1%)	60 (11.9%)	506 (100%)	961 (87.8%)	133 (12.2%)	1,094 (100%)
Nursing Assistant	1,560 (94.0%)	99 (6.0%)	1,659 (100%)	1,133 (91.9%)	100 (8.1%)	1,233 (100%)	2,693 (93.1%)	199 (6.9%)	2,892 (100%)
Nursing Aide	6,287 (95.9%)	270 (4.1%)	6,557 (100%)	4,009 (93.1%)	297 (6.9%)	4,306 (100%)	10,296 (94.8%)	567 (5.2%)	10,863 (100%)
Hospital support staff	2,012 (96.0%)	83 (4.0%)	2,095 (100%)	1,721 (94.8%)	95 (5.2%)	1,816 (100%)	3,733 (95.4%)	178 (4.6%)	3,911 (100%)
Medical Student	406 (97.1%)	12 (2.9%)	418 (100%)	100 (99.0%)	1 (1.0%)	101 (100%)	506 (97.5%)	13 (2.5%)	519 (100%)
Nursing Student	1,287 (94.6%)	74 (5.4%)	1,361 (100%)	1,036 (95.6%)	48 (4.4%)	1,084 (100%)	2,323 (95.0%)	122 (5.0%)	2,445 (100%)
Visitor	1,178 (96.5%)	43 (3.5%)	1,221 (100%)	300 (92.6%)	24 (7.4%)	324 (100%)	1,478 (95.7%)	67 (4.3%)	1,545 (100%)
Ward type									
Non-ICU wards	20,839 (93.3%)	1,497 (6.7%)	22,336 (100%)	14,698 (91.4%)	1,391 (8.6%)	16,089 (100%)	35,537 (92.5%)	2,888 (7.5%)	38,425 (100%)
ICU wards	10,115 (83.6%)	1,979 (16.4%)	12,094 (100%)	5,609 (85.5%)	948 (14.5%)	6,557 (100%)	15,724 (84.3%)	2,927 (15.7%)	18,651 (100%)

Table 5.3: Descriptive opportunity for hand hygiene by characteristics and covariates in the study (cont.)

Variable	Before intervention n (%)			After intervention n (%)			Overall n (%)		
	Not performed	Performed	Total	Not performed	Performed	Total	Not performed	Performed	Total
Department									
Obstetrics and gynecology	662 (96.9%)	21 (3.1%)	683 (100%)	2,569 (93.1%)	191 (6.9%)	2,760 (100%)	3,231 (93.8%)	212 (6.2%)	3,443 (100%)
Eye	120 (68.6%)	55 (31.4%)	175 (100%)	558 (71.0%)	228 (29.0%)	786 (100%)	678 (70.6%)	283 (29.4%)	961 (100%)
Ear Nose Throat	223 (91.8%)	20 (8.2%)	243 (100%)	504 (86.2%)	81 (13.8%)	585 (100%)	727 (87.8%)	101 (12.2%)	828 (100%)
Paediatrics	2,822 (82.6%)	596 (17.4%)	3,418 (100%)	4,105 (85.4%)	699 (14.6%)	4,804 (100%)	6,927 (84.2%)	1,295 (15.8%)	8,222 (100%)
Medicine	10,255 (92.6%)	816 (7.4%)	11,071 (100%)	6,969 (93.6%)	480 (6.4%)	7,449 (100%)	17,224 (93.0%)	1,296 (7.0%)	18,520 (100%)
Surgery	16,872 (89.6%)	1,968 (10.4%)	18,840 (100%)	5,602 (89.5%)	660 (10.5%)	6,262 (100%)	22,474 (89.5%)	2,628 (10.5%)	25,102 (100%)
Indication for performing hand hygiene									
Before touching a patient	7,516 (95.1%)	388 (4.9%)	7,904 (100%)	4,440 (92.5%)	362 (7.5%)	4,802 (100%)	11,956	750	12,706 (100%)
After touching a patient	7,012 (90.1%)	769 (9.9%)	7,781 (100%)	4,192 (89.2%)	505 (10.8%)	4,697 (100%)	11,204	1,274	12,478 (100%)
Before clean/aseptic procedures	3,679 (86.2%)	587 (13.8%)	4,266 (100%)	2,238 (85.9%)	366 (14.1%)	2,604 (100%)	5,917	953	6,870 (100%)
After body fluid exposure/risk	3,726 (77.9%)	1,054 (22.1%)	4,780 (100%)	2,133 (79.9%)	535 (20.1%)	2,668 (100%)	5,859	1,589	7,448 (100%)
After touching patient surroundings	9,021 (93.0%)	678 (7.0%)	9,699 (100%)	7,304 (92.7%)	571 (7.3%)	7,875 (100%)	16,325	1,249	17,574 (100%)

Figure 5.5: Hand-hygiene compliance in each ward by week. The white line shows the actual week when the intervention was initiated.

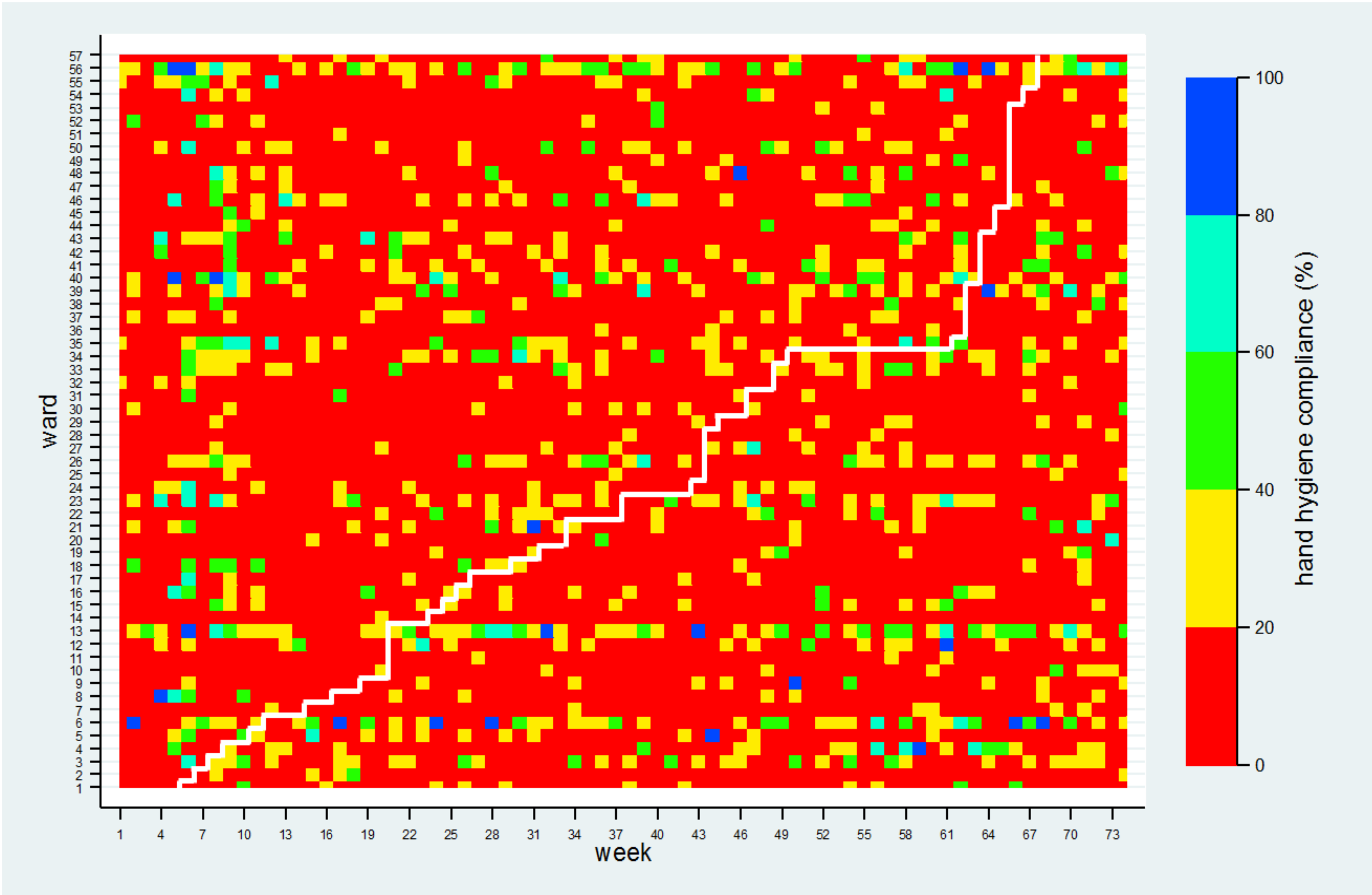


Table 5.4: Descriptive statistics for characteristics and covariates in the study by observed HCWs [n]

Variables	Overall (n = 3,272)	Overall (%)
Sex		
Male	1,039	31.75
Female	2,233	68.25
Type of HCWs		
Doctor	461	14.09
Registered Nurse	970	29.65
Technical Nurse	35	1.07
Nursing Assistant	60	1.83
Nursing Aide	288	8.8
Hospital supported staff	208	6.36
Medical Student	147	4.49
Nursing Student	644	19.68
Visitor	459	14.03
Ward type		
Non-ICU wards	2,219	67.82
ICU wards	1,053	32.18
Department		
Obstetrics and gynecology	216	6.6
Eye	45	1.38
Ear Nose Throat	50	1.53
Paediatrics	517	15.8
Medicine	1,084	33.13
Surgery	1,360	41.56

Overall impact of the intervention

In the primary intention-to-intervene analysis the intervention was associated with an improvement in hand hygiene compliance, but the effect was small (Odds ratio [OR] 1.12; 95% confidence interval [CI] 1.01 to 1.24, p = 0.027) (Table 5.5). Overall hand hygiene compliance rates were similar during the pre-intervention phase (10.09% [3,467/34,434]) and during the post-intervention phase (10.33% [2,339/22,642]).

The majority of hand hygiene compliance rates observed were less than 20% (shown in red in Figure 5.5) with similar hand hygiene compliance before and after the actual intervention date (the white line indicates the actual time the intervention was initiated in each ward).

In the first six months of the study, the rate of hand hygiene compliance differed slightly between those wards which had implemented the intervention and those which hadn't, while the rate of hand hygiene compliance was similar between these two groups of wards in the last six month of intervention period (Figure 5.6 and Figure 5.7).

Table 5.5: Estimated odds ratios (95% CI) associated with the intervention allowing for effect modification by individual ward in a model excluding potential confounders (intention-to-intervene analysis)

Factor	Estimated odds ratio	95% CI	P value
Before randomisation	Reference		
After randomisation	1.12	1.01 to 1.24	0.027
Week number	1.01	1.01 to 1.02	<0.001
Week after randomisation	1.00	1.00 to 1.01	0.314

Per-protocol analysis in implementing wards showed similar findings to the intention-to intervene analysis (OR 1.11; 95% CI 1.00 to 1.22, p = 0.043) (Table 5.6). From 57 wards of this analysis, hand hygiene compliance was observed at a similar rate during the intervention (10.22% [1,935/18,932] vs. 10.45% [2,008/19,210]).

Table 5.6: Estimated odds ratios (95% CI) of hand hygiene compliance associated with the intervention allowing for effect modification by individual ward (per-protocol analysis)

Factor	**Estimated odds ratio**	**95% CI**	**P value**
Before implementation	Reference		
After implementation	1.11	1.00 to 1.22	0.043
Week number	1.01	1.01 to 1.02	<0.001
Week after implementation	1.00	1.00 to 1.00	0.535

Impact of the intervention in ICU and non-ICU wards

The rates of hand hygiene compliance in ICU wards were slightly higher than non-ICU wards (Figure 5.6 and Table 5.7).

In the initial intention-to-intervene analysis the estimated odds ratio for an increase in hand hygiene compliance between ICU wards (OR 1.07; 95% CI 0.93 to 1.24, p = 0.335) and non-ICU wards (OR 1.15; 95% CI 1.00 to 1.33, p = 0.048) was found to be similar.

Table 5.7: Estimated odds ratios (95% CI) of hand hygiene compliance associated with the intervention allowing for effect modification by intensive-care unit in a model excluding potential confounders (intention-to-intervene analysis)

Factor	Estimated odds ratio	95% CI	P value
Non-ICU wards			
Before randomisation	Reference		
After randomisation	1.15	1.00 to 1.33	0.048
Week number	1.01	1.00 to 1.02	0.004
Week after randomisation	1.00	1.00 to 1.01	0.136
ICU wards			
Before randomisation	Reference		
After randomisation	1.07	0.93 to 1.24	0.335
Week number	1.01	1.00 to 1.02	0.059
Week after randomisation	1.00	0.99 to 1.00	0.612

Per-protocol analysis in impelmenting wards showed similar effect of the intervention on hand hygiene compliance in ICU wards (OR 1.13; 95% CI 0.97 to 1.31, p = 0.126) and non-ICU wards (OR 1.11; 95% CI 0.97 to 1.26, p = 0.146) (Table 5.8).

Table 5.8: Estimated odds ratios (95% CI) of hand hygiene compliance associated with the intervention allowing for effect modification by intensive-care unit (per-protocol analysis)

Factor	Estimated odds ratio	95% CI	P value
Non-ICU wards			
Before implementation	Reference		
After implementation	1.11	0.97 to 1.26	0.146
Week number	1.02	1.01 to 1.03	<0.001
Week after implementation	1.00	0.99 to 1.00	0.821
ICU wards			
Before implementation	Reference		
After implementation	1.13	0.97 to 1.31	0.126
Week number	1.01	1.00 to 1.02	0.046
Week after implementation	1.00	0.99 to 1.00	0.129

Figure 5.6: Hand-hygiene compliance in ICU wards (left panel) and non-ICU wards (right panel): intention-to-intervene analysis

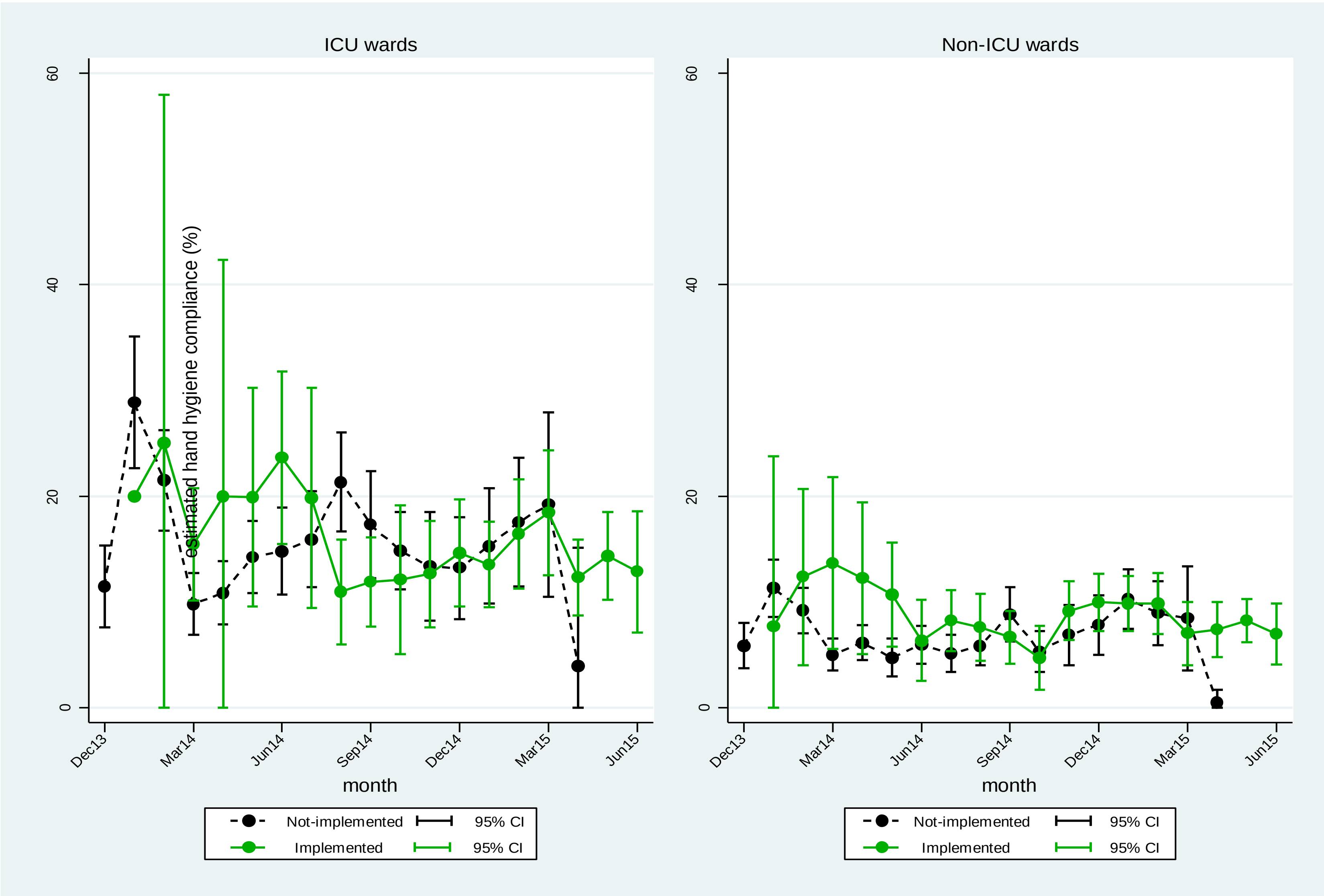
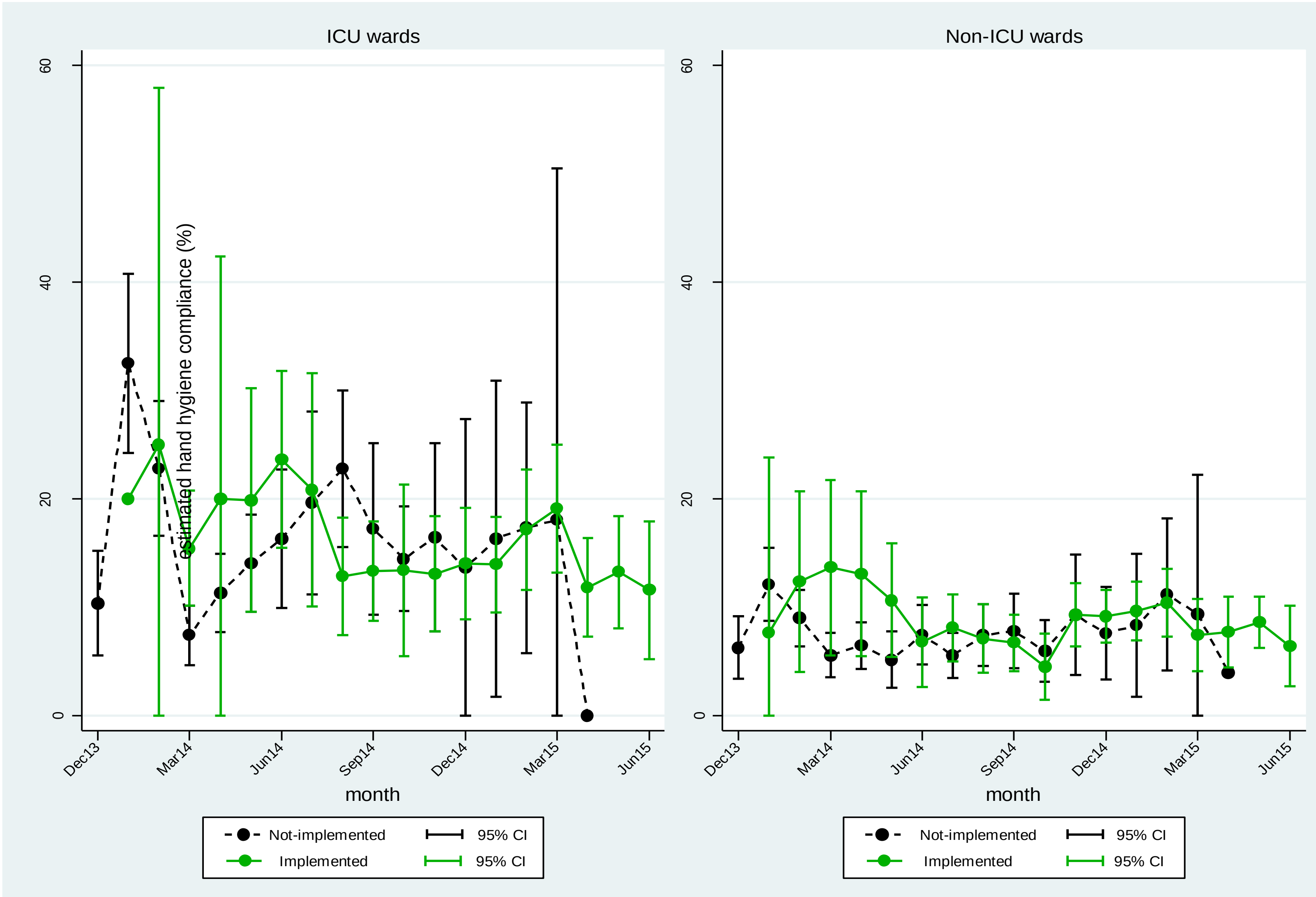


Figure 5.7: Hand-hygiene compliance in ICU wards (left panel) and non-ICU wards (right panel): per-protocol analysis



Impact of the intervention by department

The rate of hand hygiene was diffent in different departments. In the intention-to-intervene analysis, estimated odds ratios of the intervention allowing for effect modification by department, showed that the highest estimated odds ratio associated with the intervention was in the department of obstetrics and gynecology where there was evidence of a substantial increase in hand hygiene compliance (OR 3.96; 95% CI 1.88 to 8.31, $p<0.001$). A substantial positive effect was also seen in the department of paediatrics, while the lowest impact was found in the department of medicine where compliance declined (OR 0.78; 95% CI 0.61 to 0.99, $p = 0.044$) (Table 5.9).

Per-protocol analysis in impelmenting wards estimated odds ratios of the intervention allowing for effect modification by department and showed smaller effects than the result of the intention-to-intervene analysis for the department of obstetrics and gynecology (OR 2.43; 95% CI 1.05 to 5.63, $p = 0.038$), but a higher effect was found in the department of medicine (OR 0.82; 95% CI 0.66 to 1.02, $p = 0.078$) (Table 5.10).

Table 5.9: Estimated odds ratios (95% CI) of hand hygiene compliance associated with the intervention allowing for effect modification by department –subgroup analysis (intention-to-intervene analysis)

Factor	Estimated odds ratio	95% CI	P value
Department of Obstetrics and gynecology			
Before randomisation	Reference		
After randomisation	3.96	1.88 to 8.31	<0.001
Week number	0.97	0.91 to 1.04	0.384
Week after randomisation	1.04	0.97 to 1.11	0.258
Department of Paediatrics			
Before randomisation	Reference		
After randomisation	1.71	1.18 to 2.48	0.005
Week number	0.98	0.95 to 1.03	0.465
Week after randomisation	1.04	0.99 to 1.08	0.110
Department of Medicine			
Before randomisation	Reference		
After randomisation	0.78	0.61 to 0.99	0.044
Week number	1.00	0.99 to 1.02	0.576
Week after randomisation	0.99	0.98 to 1.00	0.065
Department of Surgery			
Before randomisation	Reference		
After randomisation	1.07	0.89 to 1.30	0.460
Week number	1.01	1.01 to 1.02	0.004
Week after randomisation	1.01	1.00 to 1.02	0.290

Table 5.10: Estimated odds ratios (95% CI) of hand hygiene compliance associated with the intervention allowing for effect modification by department –subgroup analysis (per-protocol analysis)

Factor	Estimated odds ratio	95% CI	P
Department of Obstetrics and gynecology			
Before implementation	Reference		
After implementation	2.43	1.05 to 5.63	0.03
Week number	1.00	0.95 to 1.06	0.96
Week after implementation	1.01	0.97 to 1.06	0.63
Department of Paediatrics			
Before implementation	Reference		
After implementation	1.18	0.93 to 1.50	0.17
Week number	1.02	1.01 to 1.04	0.00
Week after implementation	1.00	0.99 to 1.00	0.43
Department of Medicine			
Before implementation	Reference		
After implementation	0.82	0.66 to 1.02	0.07
Week number	1.00	0.99 to 1.01	0.94
Week after implementation	0.99	0.98 to 1.00	0.10
Department of Surgery			
Before implementation	Reference		
After implementation	1.12	0.93 to 1.35	0.23
Week number	1.02	1.01 to 1.03	<0.0
Week after implementation	1.00	0.99 to 1.01	0.53

5.3.4 Hand hygiene compliance by "My five moments for hand hygiene"

The most commonly observed moment for hand hygiene was the indication of 'after touching patient surroundings' (30.79% [17,574/57,076]), followed by the indication of 'before touching a patient' (22.26% [12,706/57,076]) (Table 5.3).

In intention-to-treat analysis, the highest effects of the intervention were found in the indication 'before touching a patient' with an estimated odds ratio of 1.73 (95% CI 1.32 to 2.25, p<0.001), while the smallest effect was found in the indication 'after body fluid exposure/risk' with an estimated odds ratio of 0.97 (95% CI 0.78 to 1.20, p = 0.752). Table 5.11 shows the estimated odds ratios for hand hygiene compliance according to the specific moment under the intention-to-intervene analysis.

Per-protocol analysis in implementing wards adjusting for indication for hand hygiene showed a similar finding in the estimated odds of hand hygiene compliance. Table 5.12 shows the estimated odds ratio for hand hygiene compliance according the hand hygiene moment under the per-protocol analysis.

Table 5.11: Estimated odds ratios (95% CI) for hand hygiene compliance associated with the intervention according to hand hygiene opportunity type (intention-to-intervene analysis)

Factor	Estimated odds ratio	95% CI	P value
Before touching a patient			
Before randomisation	Reference		
After randomisation	1.72	1.32 to 2.25	<0.001
Week number	1.01	0.99 to 1.03	0.451
Week after randomisation	1.00	0.99 to 1.01	0.572
After touching a patient			
Before randomisation	Reference		
After randomisation	1.09	0.89 to 1.35	0.397
Week number	1.00	0.99 to 1.01	0.862
Week after randomisation	1.01	1.00 to 1.01	0.305
Before clean/aseptic procedures			
Before randomisation	Reference		
After randomisation	1.17	0.90 to 1.52	0.234
Week number	1.02	0.99 to 1.05	0.114
Week after randomisation	1.01	1.00 to 1.03	0.151
After body fluid exposure/risk			
Before randomisation	Reference		
After randomisation	0.97	0.78 to 1.20	0.752
Week number	1.02	1.00 to 1.03	0.045
Week after randomisation	1.00	0.99 to 1.02	0.545
After touching patient surroundings			
Before randomisation	Reference		
After randomisation	1.06	0.87 to 1.28	0.569
Week number	1.01	1.00 to 1.03	0.051
Week after randomisation	0.99	0.98 to 1.00	0.100

Table 5.12: Estimated odds ratios (95% CI) for hand hygiene compliance associated with the intervention according to hand hygiene opportunity type (per-protocol analysis)

Factor	Estimated odds ratio	95% CI	P value
Before touching a patient			
Before implementation	Reference		
After implementation	1.44	1.11 to 1.86	0.006
Week number	1.01	1.00 to 1.03	0.133
Week after implementation	0.99	0.99 to 1.00	0.254
After touching a patient			
Before implementation	Reference		
After implementation	1.06	0.86 to 1.31	0.579
Week number	1.00	0.99 to 1.02	0.519
Week after implementation	1.00	0.99 to 1.01	0.887
Before clean/aseptic procedures			
Before implementation	Reference		
After implementation	1.22	0.94 to 1.58	0.141
Week number	1.03	1.00 to 1.06	0.076
Week after implementation	1.00	0.99 to 1.02	0.689
After body fluid exposure/risk			
Before implementation	Reference		
After implementation	0.99	0.79 to 1.23	0.921
Week number	1.02	1.01 to 1.03	0.019
Week after implementation	1.00	0.99 to 1.01	0.495
After touching patient surroundings			
Before implementation	Reference		
After implementation	1.07	0.88 to 1.30	0.491
Week number	1.01	1.00 to 1.02	0.088
Week after implementation	1.00	0.99 to 1.00	0.296

5.3.5 Effectiveness of a multimodal hand hygiene improvement strategy

All 57 wards (100%) implemented the intervention by applying the 'system change' and the 'reminders in the workplace'. Only four wards implemented the intervention by applying the 'institutional safety climate'. Only two wards implemented the intervention by applying all five multimodal hand hygiene improvement strategies during the study (Table 5.13).

Table 5.13: The intervention implementation by applying multimodal hand hygiene improvement strategy

Factors	**Total wards**	**%**
System Change	57	100
Training / Education	27	47.37
Evaluation and feedback	38	66.67
Reminders in the workplace	57	100
Institutional safety climate	4	7.02

Analysis in implementing wards showed the strongest association after implementing the component of 'Reminders in workplace' with an estimated odds ratio of 2.55 (95% CI 1.62 to 4.01, p<0.001). This component was implemented in all implemented wards by the research team proving a set of visual reminders and education to all implementing wards as study materials including posters, leaflets, flipcharts and video that covered (i) my 5 moments for hand hygiene; (ii) handwashing/handrubbing steps; (iii) gloves using; (iv) transmission of healthcare associated pathogens; and (v) impact of HCAI. The component of 'Training / Education' provided the lowest association with an estimated odds ratio of 0.89 (95% CI 0.76 to 1.04, p=134) (Table 5.14).

Table 5.14: Estimated odds ratios (95% CI) for hand hygiene compliance associated with the intervention components

Factor	Estimated odds ratio	95% CI	P value
Before randomisation	Reference		
System Change	1.05	0.95 to 1.19	0.317
Training / Education	0.89	0.76 to 1.04	0.134
Evaluation and feedback	1.24	1.07 to 1.44	0.004
Reminders in the workplace	2.55	1.62 to 4.01	<0.001
Institutional safety climate	1.44	1.10 to 1.88	0.007

5.4 Discussion

5.4.1 Key findings

The principle findings of this trial were that a multimodal hand hygiene improvement intervention, designed using a stepped wedge randomized control design with active engagement of ward staff in designing the action plan to induce behaviour change in ward level, produced a small improvement in hand hygiene in both intention-to intervene and per-protocol analyses.

The reasons for the quite disappointing levels of improvement might come from the several difficulties of implementation, including factors at the ward and hospital level. Some evidence of clinically significant improvements in individual wards is found, and this could be related with greater success in changing the ward-based culture or high-level co-operation in the ward from all ward staff.

To our knowledge, this is the first randomized controlled trial applying the WHO hand hygiene intervention outside high income countries. While the improvements were small, and probably of limited overall clinical significance, the study establishes the feasibility to apply the WHO strategy to promote hand hygiene in resource limited settings and also suggests the need for more active engagement from administrators in making, prioritizing and integrating the action plan into standard policies.

5.4.2 Comparison of findings with other studies

The difficulties in implementing the intervention as planned are consistent with the findings of the FIT study by Fuller *et al.*[108], which reported that infection control at the ward was perceived as having lower priority than other work. The difficulty for delivering the intervention comes from several reasons including individual reasons (knowledge, wrong beliefs on hand hygiene, awareness, emotion) and institutional reasons reasons (lacking of supplies, staffing, and high workload).

Several studies have proposed that ward-based or team –based strategies could be a key strategy to promote hand hygiene by taking advantage of the social context of each setting and it has been claimed that this approach is underpinned by theories from behavioural science. [196] This idea suggests that greater success in implementation of the intervention could be achieved if there were an action plan focusing on each ward and holding workshops to discuss the workflow of each ward to make a ward-specific plan.[196] Following this suggestion Huis *et al.* found high improvement in particular wards that were successful in making culture changes at the ward to make staff more aware of performing hand hygiene. In this study, there were also examples of creative idea to promote hand hygiene. For example, some wards set a hand hygiene day in every month. On these days there were activities to promote hand hygiene in the ward in a similar manner to the annual hospital hand hygiene day (activities included reminders between HCWs and education and practice sessions). Other wards had representatives of each HCW type involved in the design of the action plan to promote hand hygiene in their role.

Comparative efficacy of the WHO strategy to promote hand hygiene in hospitals between 1980 and 2009 is reported in a systemic review by Luangasanatip *et al.*[82], which analysed data from high quality intervention studies (including randomized controlled trials, interrupted time series, non-randomized trials, and controlled before-after studies). Network meta-analysis from this review indicated considerable uncertainty in the relative effectiveness of interventions, but nonetheless provided evidence that WHO strategy is effective and that compliance can be further improved by adding interventions including goal setting, reward incentives, and accountability. [82] In some successful wards in this study, goal-setting was used as an additional intervention: two wards chose to have routine meetings to evaluate the intervention plan, revise the goals and plan to achieve the target rates of hand hygiene.

5.4.3 Strengths, limitations and future directions

The principle strength of the study is the strong design used to evaluate the impact of the WHO strategy: by using a stepped wedge design each ward compares their own compliance at different time points, pre and post- intervention. [108, 193] This design, a type of cluster randomized trial, also meets requirements of the previous systematic review of high quality studies.[82, 103] This study also implemented the intervention hospital-wide in a resource limited hospital, while most previous studies from LMICs have evaluated interventions only in more restricted study populations.

The study's main limitation was that the intervention was more difficult to implement than anticipated despite high level support for the intervention in the hospital. Two other studies have mentioned a lack of concern or belief in hand hygiene being able to prevent HCAI as a main source of difficulty.[197, 198] This appears to be one of the difficulties of this study as well, based on the qualitative research described in the previous chapters. In another study, the impact of a team and leaders-directed strategy to improve hand hygiene was evaluated in a cluster randomized controlled trial. This proved to be successful in improving hand hygiene but the authors also reported the difficulties in the participating wards due to higher priority work.[196] Such competing priorities were likely a key issue in this study as well, and were one reason for the delays in the intervention. Intervention to improve hand hygiene compliance (or maintain it at high level) is an integral part of hospital infection control, and the hospital infection control staff is the responsible people to deliver the intervention.[108] In this study the ICT were not always able to obtain the co-operation of the majority of ward staff despite high-level endorsement of the intervention by the hospital director. This is likely to be a key reason the intervention was not successful at achieving larger improvements in hand hygiene.

A second limitation was the possibility of contamination between clusters, which might be occurring. As a results of the meeting the infection control ward nurses are attending every month, there is a chance of contamination occurring. This would be expected to result in overall increases in compliance over time, but might lead to smaller differences between pre- and post-intervention periods in implementing wards.

A final limitation was the difficulty in the wards self-reporting of the specific intervention measures they had taken, which was consistently poor.

Future analysis of the data collected in this study needs to explore factors associated with positive and negative outcomes at the ward level. Qualitative methods need to consider how successful factors in the ward-based culture act to improve hand hygiene and also consider additional interventions (goal-setting, incentives) and seek to engage higher-level decision-makers in overcoming institutional inertia. The association between hand hygiene compliance and the rate of HCAIs needs to be explored as well.

5.5 Conclusions

In conclusion, this study has evaluated an intervention that implemented the WHO Multimodal Hand Hygiene Improvement Strategy outside a high income country. The results show a small positive affect overall, though with much larger effects in some wards. They also provide information on the feasibility and difficulties of implementing the WHO strategy.

The findings from this study are intended to be generalizable to other resource-constrained hospitals in Thailand and elsewhere. Applying the WHO strategy by making ward-specific plans with involvement of the ward staff under the supervision of the infection control team led to improvements in hand hygiene behavior, though the size of these improvements was small and unlikely to translate into substantial clinical benefit. This study should provide outcomes that can inform further improvements in hand hygiene improvement strategies.

Chapter 6

Discussion and conclusions

Chapter 3-5 provided the main findings, as well as discussions and conclusions for each study in turn. This chapter summarizes the key findings, the strengths and limitation of this thesis and the overall conclusions. Future research recommendations are also considered.

6.1 Substantive discussion

Key results from the analysis of retrospective data in chapter 3 were the findings that there is a high and increasing incidence of hospital-acquired bacteraemia (HAB) and healthcare-associated bacteraemia (HCAB) in provincial hospitals in northeast Thailand, an increasing proportion of extended-spectrum beta-lactamases-producing (ESBL-producing) isolates, and very high associated mortality. This study also showed that nosocomial infection is an increasing and important problem in northeast Thailand. The total number of deaths associated with HAB and HCAB in 2010 in the study (n= 634) were much higher than the total number of reported deaths due to important notifiable diseases such as dengue hemorrhagic fever (n= 139), influenza (n= 126), and leptospirosis (n= 43) during the same period countrywide.

A key strength of this work was the use of long time series and linking of multiple routinely available databases to get a better picture of the epidemiology of HAB and HCAB in northeast Thailand. A limitation of this study is that more complete clinical data were not available. As data on process surveillance were not available, the reasons for the increased incidence of HAB could not be systematically assessed.

Although monitoring of nosocomial infection in developing countries is hampered by incomplete routine notification, this study has shown that careful evaluation of readily available routinely collected databases can provide valuable information on the incidence and trends of HAB and HCAB. The methodology used could be applied to other geographical areas where microbiological facilities are available to provide a more comprehensive global picture of the importance of nosocomial infection as a cause of death. These estimates reinforce the need for improved surveillance and prevention of nosocomial infection in similar settings.

There are a number of ways that future research could follow on from this work. In some cases, information on nosocomial infection in developing countries can be obtained by integrating readily available databases. Linking routine clinical and laboratory databases can lead to a better understanding of the burden of healthcare-associated infection (HCAI) and help infection-control practitioners better target their efforts to reduce the incidence of HCAI and associated mortality.

Although the study data showed that, in general, patients with HAB and HCAB stayed in the hospital longer than those without, the analysis did not take account of the high mortality associated with HAB and HCAB. The length of stay would be further extended if mortality in patients with HAB and HCAB could be reduced. Additional costs and extra length of stay attributable to HAB and HCAB will be further evaluated in the future using health economic models

The qualitative and quantitative work described in Chapter 4, evaluating knowledge, beliefs and practice about hand hygiene in healthcare workers represents one of the first reports applying a theoretical domain framework to identify systematically the barriers or enablers that may affect hand hygiene behaviour of HCWs in a resource limited setting. The results showed clear differences across theoretical domains at the individual level, suggesting some explanations for implementation difficulties. This study used triangulation to identify the factors associated with hand hygiene compliance, and applied a systematic approach to explore the factors associated with hand hygiene behaviour, linking these to behaviour change techniques in the intervention phase.

Limitations of this included, first, the fact that allocation of certain items to domains was not always clear. Second, some domains might have overlapping meanings that could affect the results. One example of such potential overlap is the domain social/professional role and identity and the domain social influences.

The results from this part of the thesis are important because intervention development can potentially benefit from identifying relevant domains as part of the process. When designing interventions to improve hand hygiene, target domains should not only be selected but also the relevance of each domain to behaviour change should be considered as well. Future research is needed to evaluate how these domains relate to behaviours targeted in the promotion of hand hygiene, and how various interventions can change these behaviours.

The key findings of the trial described in Chapter 5 were that a multimodal hand hygiene improvement intervention, designed using a stepped wedge cluster randomized controlled trial with active engagement of ward staff in designing the action plan to induce behaviour change at the ward level, produced a small improvement in hand hygiene in both intention-to intervene and per-protocol analyses. The reasons for the quite disappointing levels of improvement might come from the several difficulties of implementation, including factors at the ward and hospital level. Some evidence of clinically significant improvements in individual wards was, however, found. This could be related to wards having greater success in changing the ward-based culture or high-level co-operation in the ward from all ward staff.

A principle strength of the study is the strong design to evaluate the impact of the WHO strategy by using the stepped wedge design. This design allows each ward to compare their own compliance at multiple time points, before and after the intervention. The study's main limitation was that the intervention was more difficult to implement than anticipated despite high level support for the intervention in the hospital.

The results from this study are important because, to our knowledge, this is the first randomized controlled trial applying the WHO hand hygiene intervention outside high income countries. While the improvements were small, and probably of limited overall clinical significance, the study establishes the feasibility of applying the WHO strategy to promote hand hygiene in resource limited settings.

Though the overall improvements in hand hygiene were disappointing, studies such as this one which do not achieve substantial improvement are important in helping identify limitations of existing approaches to hospital hygiene, identifying obstacles to improvement, and in suggesting ways in which such obstacles may be overcome. It is therefore important to consider possible reasons that explain why only small improvements in hand hygiene compliance were seen in this study. There are two aspects to this problem.

Firstly, factors relating to the delivery of the intervention:

(1) Delays in the implementation of the intervention. Only 16 wards from 58 delivered the intervention at the time specified in the protocol (the others delivered the intervention at a later time). This resulted in reduced time to completely implement all five multimodal components of the WHO intervention. In fact, only 5 wards completely implemented all five components of the intervention.

(2) Absence of system to monitor the interventions. While the ICT had ben been requested to provide routine monthly reports about interventions in place in different wards, in practice this rarely happened, and there were no systems in place to provide incentives to the ICT team to monitor intervention delivery.

Secondly, hospital factors relating to the level of receptiveness to the intervention:

(1) The high workload of ward staff, with bed occupancy over 100 % during the study period (range from 115% to 120%), and number of beds for admissions increasing from 1,200 beds in 2013 to 1,400 beds in 2015 (without an increase in the number of wards), may have affected receptiveness to the intervention amongst hospital staff. At this hospital general wards, such as medical and surgical wards, have a low ratio of nurses to patients (approximately 1 nurse: 10 patients). Numerous studies have previously reported that high staff workload is associated with reduced hand hygiene compliance.

(2) The high workload of the ICT. At the study hospital the ICT were responsible for 70 in-patient wards, 12 out-patient wards, and 8 operation rooms. The ICT has four full-time infection control nurses (1 ICN: 300 beds). When comparing this ratio to other studies, the Study on the Efficacy of Nosocomial Infection Control (SENIC Project) recommended a ratio of one infection preventionist (IP) to 250 acute care beds in 1980[199] (only slightly below the ratio in our study). In contrast, in the United States, it is reported that there is an average of 1.2 infection preventionists (IPs) per 100 beds.[200]

(3) Lack of prioritization for hand hygiene amongst hospital staff and the ICT, and lack of priority guidelines for infection prevention and control amongst all levels of hospital staff may be an important factor in the disappointing results. A major concern of the ICT was to investigate and attempt to control perceived outbreaks (i.e. clusters of similar infections), and these activities may have taken precedence over efforts to increase basic hygiene. This suggests that recommendations from the World Health Organization that good hygiene should be at the heart of infection control and the first priority for controlling health-care associated infections had either not been effectively communicated to healthcare workers within the hospital in general and the ICT in particular or were not believed. This suggests that clear guidelines for prioritizing infection prevention control activities are needed, alongside effective interventions to communicate such guidelines to relevant staff and to ensure their implementation.[69]

Future analysis of the data collected in this study will be able to explore factors associated with positive and negative outcomes at the ward level. Qualitative methods need to consider how successful factors in the ward-based culture act to improve hand hygiene and also consider additional interventions (e.g. goal-setting, incentives) [82] and seek to engage higher-level decision-makers in overcoming institutional inertia. The association between hand hygiene compliance and the rate of HCAIs needs to be explored as well.

6.2 Implications of the research findings

The findings from chapter 3 based on linking of clinical databases, such as microbiological and admission data highlights the value of this approach for understanding the changing burden of hospital-acquired infection and multiple drug resistance (MDR) in a resource limited setting.

Such an approach is likely to be valuable in other countries as well, and could be expanded to study the epidemiology and burden of multidrug-resistant bacterial more widely.[201] This approach also provides important information for infection control programmes as it shows the current epidemiological picture and trends and can help guide the generation of future policies for infection control. This surveillance of HCAI underpins infection control activities and efforts to reduce the burden of HCAI. [202, 203]

The findings from chapter 4 provide important information that can lead to a better understanding of factors associated with non-compliance in hand hygiene behaviour. This information is important for designing and implementing interventions because it both helps to establish a baseline (of knowledge, compliance etc.) but also reveals specific problems that need to be addressed. This can help each setting to generate an action plan to promote hand hygiene. All fourteen domains of the theoretical domain framework were addressed and their effect on hand hygiene behavior considered. It is not only the pre-intervention phase that needs to identify the barriers to better hand hygiene behaviour, but also, in the intervention phase, behaviour change techniques could be applied to increase the chance of success. Other studies have already demonstrated that this approach can work, applying the behaviour change technique during the intervention and leading to real improvements.[100] The qualitative work also helped to highlight the fact that hand hygiene consumes a lot of time this may be a key barrier for better hand hygiene behaviour in this study. Several studies have demonstrated that alcohol-based handrub (ABHR) is much more effective than handwashing at decontaminating hands and killing bacteria, as well as requiring less time using than handwashing with soap and water. To address the time concern, Reilly *et al.* conducted an RCT to evaluate the microbiologic effectiveness of the World Health Organization's 6-step (WHO's 6-step) and the Centers for Disease Control and Prevention's 3-step (CDC's 3-step) hand hygiene techniques using ABHR. While the results showed that the two methods are both effective to reduce the bacteria count,[80] it also provided the first evidence in an RCT that the 6-step technique is superior, suggesting that international guidance documents should consider this evidence, as should healthcare organizations still using the 3-step technique in practice.[80]

In chapter 5, by promoting hand hygiene compliance by applying the WHO multimodal strategy with custom ward-based implementation, several difficulties to implement the intervention were found. In particular, as in previous RCTs in high income countries,[108] an important reason for this may be due to lack of concern with hand hygiene as a hospital priority and consequent lack support from the hospital administrators. However, some ward with high co-operation and good improvement were found. Ward-based promotion of hand hygiene has the potential to increase chances of success because local ward-specific challenges and opportunities can be addressed. Support from administrative staff and the infection control team are continuously needed in the process of promoting hand hygiene.[204] The linkage between improving hand hygiene and the reduction of HCAI is another reason for the need to raise the priority of hand hygiene in healthcare settings. The scientific evidence generated should also support decision making for hand hygiene interventions.[81, 205, 206]

6.3 Limitations of this thesis

There are several important limitations in this thesis.

- Firstly, we cannot easily compare benchmarks of HAB and HCAB with other settings in Thailand due to lack of clinical data, and we do not currently have data to look at rates of HAB and HCAB after 2010.
- Secondly, this study cannot assess the relationship between improving hand hygiene and HCAIs. This is because of lack of statistical power and the small effect of the intervention in improving hand hygiene.
- Thirdly, there might be contamination between the wards that have received the intervention and those that haven't, diluting the measurable intervention effect. Because all infection control ward nurses have a routine meeting every month, information from wards that have received the intervention might be shared with wards that haven't. This would be expected to lead to a reduced difference in outcomes between intervention and control groups.
- Finally, the original intention was that the ICT would be responsible for delivering the intervention to the ward staff with the intervention team including one ICT member, one member of research staff, and one ID physician. This is because the aim was to provide a generalisable intervention at minimal additional cost (and therefore no additional resources were supplied for implementing it, considering it as part of the expected duties of the infection control team). In practice, it was only in the first six months of the intervention period that the intervention was delivered by ICT. After this period the majority of the intervention was delivered jointly by research staff and the ID physician, because the ICT is fully occupied with routine hospital work.

6.4 Strengths of this thesis

Key strengths of the thesis include the use of combined data sources for enhanced epidemiological surveillance, application of a systematic theory and triangulation to explore the determinants of hand hygiene behavior, and the use a strong design (a randomized control trial) to assess the impact of hand hygiene interventions at both hospital and ward level.

6.5 Future research directions

Further analysis need to be performed to (1) determine the factors associated with any decline/increase hand hygiene compliance (day, seasonal, individual); (2) to identify the association between hand hygiene compliance and HCAI; (3) to assess the short and longer-term success of strategies to improve hand hygiene compliance and to determine whether a sustained increase in hand hygiene compliance can reduce the burden of healthcare-associated infections. Modeling could also be applied to determine factors associated with any decline/increase in compliance to reduce of healthcare-associated infection. Both qualitative research and model-based analysis of time series hand hygiene data should also be performed to identify appropriate timing for re-booting the intervention program.

In addition to recognition of the research findings, establishing methods and models for further work in LMIC settings are important outputs. The mixed method approaches employed to gain a deeper understanding of hand hygiene behaviour are increasingly being recognised as a valuable tool for helping to understand obstacles to improvements that need to be overcome. Future research could go on to use such methods to better understand how the ICT chooses to prioritize decisions with the aim of developing interventions to help them make better decisions. The burden study illustrated the great value of linking different databases, and illustrated feasible methods to capture the number of hospital-acquired infection, which have clear relevance for other settings. The intervention study was innovative both in the use of the methodologically strong stepped-wedge design and the participatory approach to intervention development. While this was associated with good improvements in hand hygiene behaviour in some wards, and these wards can be used as role models for future interventions (7 wards from 58 wards), more work needs to be done to explore how such positive outcomes could be extended to other wards. It seems likely that having systems in place to monitor and feedback intervention deployment may represent an important aspect of future work, given the low take-up of interventions. Even though this study didn't achieve substantial improvements throughout the whole hospital, examples where the intervention did appear to work may provide insights of relevance for future work. For example, one ward saw a three-fold improvement in hand hygiene, and ward staff showed evidence of working well as a team work and feeling ownership in the interventions to promote hand hygiene. In this ward, for each type of HCW there was a key leader in the ward team taking responsibility for the design and evaluation of the intervention. The benefits of such feelings of ownership have been referred to as the "IKEA effect" concept, which has previously been reported to provide good results in another study aimed at promoting antimicrobial stewardship in hospitals. [207]

6.6 Conclusions

This thesis highlights the importance of addressing the burden of HCAIs in northeast Thailand. Almost certainly the results and the methods used have wider applicability and linking available databases in other settings is likely to lead to better estimates of the burden of HCAI. It also points to ways in which HCAI can be prevented by the promotion of proper hand hygiene practice by HCWs; equally importantly, it highlights the challenges in doing this.

The compliance with recommended hand hygiene guidelines amongst healthcare workers (HCWs) was low in the study hospital, and is probably still much too low worldwide, including in Thailand. A better understanding of the factors associated with non-compliance by applying behaviour theories can play an important role in solving this problem and designing better interventions to promote hand hygiene. It is not only the individual factors that influence hand hygiene behaviour but the social context (intrapersonal, community interactions) that needs to be systematically identified.

In this study it was found that the impact of the WHO multimodal strategy was low, probably in part due to problems in fully implementing the strategy as planned. New approaches are needed to address these implementation challenges. For example, goal-setting, better support from peers (including local hand hygiene “champions”) and from administrators and the infection control team, which should act as supporter, supervisor, and monitor through the intervention. These could all play a role to ensure hand hygiene has a high priority and is performed routinely as part of standard care.

References

1. *World Health Organization.The burden of health care-associated infection worldwide [Online]. Available: http://www.who.int/gpsc/country_work/burden_hcai/en/. Accessed 7 Nov 2016.*

2. *World Health Organization. Report on the burden of endemic health care-associated infection worldwide [Online]. Available: http://apps.who.int/iris/bitstream/10665/80135/1/9789241501507_eng.pdf. Accessed 7 Nov 2016.* 2011.

3. Allegranzi, B., et al., *Burden of endemic health-care-associated infection in developing countries: systematic review and meta-analysis.* Lancet, 2011. **377**(9761): p. 228-41.

4. Allegranzi, B. and D. Pittet, *Healthcare-associated infection in developing countries: simple solutions to meet complex challenges.* Infect Control Hosp Epidemiol, 2007. **28**(12): p. 1323-7.

5. Allegranzi, B., *Healthcare associated infections. In Summary of the evidence on patient safety : implications for research.* World Health Organization, Geneva, 2008.

6. Zaidi, A.K.M., et al., *Hospital-acquired neonatal infections in developing countries.* The Lancet. **365**(9465): p. 1175-1188.

7. Pittet, D., et al., *Infection control as a major World Health Organization priority for developing countries.* Journal of Hospital Infection, 2008. **68**(4): p. 285-292.

8. Danchaivijitr, S., et al., *Prevalence of nosocomial infection in Thailand 2006.* J Med Assoc Thai, 2007. **90**(8): p. 1524-9.

9. Danchaivijitrmd, S., et al., *Prevalence and impacts of nosocomial infection in Thailand 2001.* J Med Assoc Thai, 2005. **88 Suppl 10**: p. S1-9.

10. Huang, S.S., et al., *Targeted versus universal decolonization to prevent ICU infection.* N Engl J Med, 2013. **368**(24): p. 2255-65.

11. Pronovost, P., et al., *An intervention to decrease catheter-related bloodstream infections in the ICU.* N Engl J Med, 2006. **355**(26): p. 2725-32.

12. Nickerson, E.K., et al., *Factors predicting and reducing mortality in patients with invasive Staphylococcus aureus disease in a developing country.* PLoS One, 2009. **4**(8): p. e6512.

13. Nickerson, E.K., et al., *Meticillin-resistant Staphylococcus aureus in rural Asia.* Lancet Infect Dis, 2006. **6**(2): p. 70-1.

14. Nickerson, E.K., et al., *Staphylococcus aureus bacteraemia in a tropical setting: patient outcome and impact of antibiotic resistance.* PLoS One, 2009. **4**(1): p. e4308.

15. Mekviwattanawong, S., et al., *Epidemiology of Staphylococcus aureus infections and the prevalence of infection caused by community-acquired methicillin-resistant Staphylococcus aureus in hospitalized patients at Siriraj Hospital.* J Med Assoc Thai, 2006. **89 Suppl 5**: p. S106-17.

16. *World Health Organization. Summary of the evidence on patient safety: implications for research.* 2008.

17. Allegranzi, B. and D. Pittet, *Role of hand hygiene in healthcare-associated infection prevention.* Journal of Hospital Infection, 2009. **73**(4): p. 305-315.

18. Pittet, D., et al., *Effectiveness of a hospital-wide programme to improve compliance with hand hygiene.* The Lancet, 2000. **356**(9238): p. 1307-1312.

19. Larson, E.L., et al., *An organizational climate intervention associated with increased handwashing and decreased nosocomial infections.* Behav Med, 2000. **26**(1): p. 14-22.

20. Watanakunakorn, C., C. Wang, and J. Hazy, *An observational study of hand washing and infection control practices by healthcare workers.* Infect Control Hosp Epidemiol, 1998. **19**(11): p. 858-60.

21. Pittet, D., *Improving adherence to hand hygiene practice: a multidisciplinary approach.* Emerg Infect Dis, 2001. **7**(2): p. 234-40.

22. Pittet, D., *Improving compliance with hand hygiene in hospitals.* Infect Control Hosp Epidemiol, 2000. **21**(6): p. 381-6.

23. Pittet, D., et al., *Hand hygiene among physicians: performance, beliefs, and perceptions.* Ann Intern Med, 2004. **141**(1): p. 1-8.

24. Hugonnet, S., T.V. Perneger, and D. Pittet, *Alcohol-based handrub improves compliance with hand hygiene in intensive care units.* Arch Intern Med, 2002. **162**(9): p. 1037-43.

25. Danchaivijitr, S., et al., *Strategies to improve hand hygiene practices in two university hospitals.* J Med Assoc Thai, 2005. **88 Suppl 10**: p. S155-60.

26. Lam, B.C., J. Lee, and Y.L. Lau, *Hand hygiene practices in a neonatal intensive care unit: a multimodal intervention and impact on nosocomial infection.* Pediatrics, 2004. **114**(5): p. e565-71.

27. Pittet, D., et al., *The World Health Organization Guidelines on Hand Hygiene in Health Care and Their Consensus Recommendations.* Infection Control and Hospital Epidemiology, 2009. **30**(7): p. 611-622.

28. Yuan, C.T., et al., *Perceptions of hand hygiene practices in China.* Journal of Hospital Infection, 2009. **71**(2): p. 157-162.

29. Borg, M.A., et al., *Health care worker perceptions of hand hygiene practices and obstacles in a developing region.* American Journal of Infection Control, 2009. **37**(10): p. 855-857.

30. Joshi, S.C., et al., *Qualitative study on perceptions of hand hygiene among hospital staff in a rural teaching hospital in India.* Journal of Hospital Infection, 2012. **80**(4): p. 340-344.

31. Pittet, D., B. Allegranzi, and J. Storr, *The WHO Clean Care is Safer Care programme: field-testing to enhance sustainability and spread of hand hygiene improvements.* J Infect Public Health, 2008. **1**(1): p. 4-10.

32. Wendt, C., D. Knautz, and H.v. Baum, *Differences in Hand Hygiene Behavior Related to the Contamination Risk of Healthcare Activities in Different Groups of Healthcare Workers.* Infection Control and Hospital Epidemiology, 2004. **25**(3): p. 203-206.

33. Whitby, M., M.-L. McLaws, and M.W. Ross, *Why Healthcare Workers Don't Wash Their Hands: A Behavioral Explanation.* Infection Control & Hospital Epidemiology, 2006. **27**(05): p. 484-492.
34. O'Boyle, C.A., S.J. Henly, and E. Larson, *Understanding adherence to hand hygiene recommendations: The theory of planned behavior.* American Journal of Infection Control, 2001. **29**(6): p. 352-360.
35. Trunnell, E.P. and G.L. White, Jr., *Using behavior change theories to enhance hand hygiene behavior.* Educ Health (Abingdon), 2005. **18**(1): p. 80-4.
36. Francis, J.J., D. O'Connor, and J. Curran, *Theories of behaviour change synthesised into a set of theoretical groupings: introducing a thematic series on the theoretical domains framework.* Implementation Science : IS, 2012. **7**: p. 35-35.
37. Michie, S., M.M. van Stralen, and R. West, *The behaviour change wheel: A new method for characterising and designing behaviour change interventions.* Implementation Science : IS, 2011. **6**: p. 42-42.
38. Green, S., et al., *Using a theoretical framework to identify barriers and enablers to the uptake of an evidence-based clinical practice guideline in general practice*. 2008.
39. Francis, J.J., et al., *Using theories of behaviour to understand transfusion prescribing in three clinical contexts in two countries: Development work for an implementation trial.* Implement Sci, 2009. **4**.
40. *Developing and evaluating complex interventions: new guidance*. 2008, London: MRC.
41. Campbell, M., et al., *Framework for design and evaluation of complex interventions to improve health.* BMJ, 2000. **321**.
42. Michie, S., et al., *Making psychological theory useful for implementing evidence based practice: a consensus approach.* Qual Saf Health Care, 2005. **14**(1): p. 26-33.
43. Lippke, S. and J.P. Ziegelmann, *Theory-based health behavior change: developing, testing, and applying theories for evidence-based interventions.* Appl Psychol, 2008. **57**.

44. Ashford, A.J., *Behavioural change in professional practice: supporting the development of effective implementation strategies*. 1998.

45. Improved Clinical Effectiveness through Behavioural Research, G., *Designing theoretically-informed implementation interventions.* Implement Sci, 2006. **1**: p. 4.

46. *World Health Organization. A Guide to the Implementation of the WHO Multimodal Hand Hygiene Improvement Strategy. [Online]. Available: http://www.who.int/gpsc/5may/Guide_to_Implementation.pdf. Accessed 7 Nov 2016*. 2009.

47. *WHO Guidelines on Hand Hygiene in Health Care. First Global Patient Safety Challenge Clean Care is Safer Care. [Online]. Available: http://apps.who.int/iris/bitstream/10665/44102/1/9789241597906_eng.pdf. Accessed 7 Nov 2016*. 2009.

48. Castro-Sanchez, E. and A. Holmes, *International implementation of WHO's hand hygiene strategy.* Lancet Infect Dis, 2013. **13**(10): p. 824-5.

49. Allegranzi, B., *Successful implementation of the World Health Organization hand hygiene improvement strategy in a referral hospital in Mali, Africa'.* Infect Control Hosp Epidemiol, 2010. **31**.

50. Allegranzi, B., *Global implementation of WHO's multimodal strategy for improvement of hand hygiene: a quasi-experimental study'.* Lancet Infect Dis, 2013. **13**.

51. Schmitz, K., *Effectiveness of a multimodal hand hygiene campaign and obstacles to success in Addis Ababa, Ethiopia'.* Antimicrob Resist Infect Control, 2014. **3**.

52. Garner, J.S., et al., *CDC definitions for nosocomial infections, 1988.* American Journal of Infection Control. **16**(3): p. 128-140.

53. *Prevention of hospital-acquired infections: a practical guide. Geneva: World Health Organization.* 2002.

54. Horan, T.C., M. Andrus, and M.A. Dudeck, *CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting.* Am J Infect Control, 2008. **36**(5): p. 309-32.

55. *National Institute for Health and Care Excellence. Healthcare-associated infections: prevention and control.* 2011.

56. Morin, C.A. and J.L. Hadler, *Population-based incidence and characteristics of community-onset Staphylococcus aureus infections with bacteremia in 4 metropolitan Connecticut areas, 1998.* J Infect Dis, 2001. **184**(8): p. 1029-34.

57. Friedman, N.D., et al., *Health care--associated bloodstream infections in adults: a reason to change the accepted definition of community-acquired infections.* Ann Intern Med, 2002. **137**(10): p. 791-7.

58. Siegman-Igra, Y., et al., *Reappraisal of community-acquired bacteremia: a proposal of a new classification for the spectrum of acquisition of bacteremia.* Clin Infect Dis, 2002. **34**(11): p. 1431-9.

59. Shorr, A.F., et al., *Healthcare-associated bloodstream infection: A distinct entity? Insights from a large U.S. database.* Crit Care Med, 2006. **34**(10): p. 2588-95.

60. *World Health Organisation. Hospital hygiene and infection control [Online]. Available: http://www.who.int/water_sanitation_health/medicalwaste/148to158.pdf. Accessed on 15 January 2017.*

61. *World Health Organization.Safe Management of Wastes from Health-care Activities [Online]. Available: http://www.who.int/injection_safety/toolbox/docs/en/waste_management.pdf. Accessed 1 Jun 2017.* 1999.

62. Coia, J.E., A.T. Leanord, and J. Reilly, *Screening for meticillin resistant Staphylococcus aureu (MRSA)_who, when, and how?* BMJ : British Medical Journal, 2014. **348**.

63. Pittet, D., et al., *Evidence-based model for hand transmission during patient care and the role of improved practices.* Lancet Infect Dis, 2006. **6**(10): p. 641-52.

64. *World Health Organization. WHO guidelines for hand hygiene in health care*, in *WHO Guidelines on Hand Hygiene in Health Care: First Global Patient Safety Challenge Clean Care Is Safer Care*. 2009: Geneva.

65. *Centers for Disease Control and Prevention. Guidance Documents [Online] Avialable: https://www.cdc.gov/hicpac/recommendations/index. Accessed 15 April 2016.*

66. Loveday, H.P., et al., *epic3: national evidence-based guidelines for preventing healthcare-associated infections in NHS hospitals in England.* J Hosp Infect, 2014. **86 Suppl 1**: p. S1-70.

67. *National Institute for Health and Care Excellence (NICE). Improving health and social care through evidence-based guidance [Online] Avialable: https://www.nice.org.uk/. Accessed 15 April 2016.*

68. *World Health Organization. Practical Guidelines fos infection Control in Health Care Facilities [Online] Avialable: http://www.wpro.who.int/publications/docs/practical_guidelines_infection_control.pdf. Accessed 15 April 2016.*

69. Danchaivijitr, S., et al., *Quality of nosocomial infection control in Thailand.* J Med Assoc Thai, 2005. **88 Suppl 10**: p. S145-9.

70. Danchaivijitr, S., et al., *Problems and obstacles in implementation of nosocomial infection control in Thailand.* J Med Assoc Thai, 2005. **88 Suppl 10**: p. S70-4.

71. Buachum, S., et al., *Nosocomial infection control in regional and provincial hospitals.* J Med Assoc Thai, 2005. **88 Suppl 10**: p. S124-7.

72. Picheansathian, W., A. Pearson, and P. Suchaxaya, *The effectiveness of a promotion programme on hand hygiene compliance and nosocomial infections in a neonatal intensive care unit.* International Journal of Nursing Practice, 2008. **14**(4): p. 315-321.

73. *Prevention of Healthcare Associated Infections (HAIs) in the Medical Office [Online]. Available: https://www.magmutual.com/prevention-healthcare-associated-infections-hais-medical-office. Accessed 1 Jun 2016.*

74. *Ontario Agency for Health Protection and Promotion (Public Health Ontario). Provincial Infectious Diseases Advisory Committee. Best practices for hand hygiene in all health care settings.*

5th ed. Toronto: Queen's Printer for Ontario. 2014.

75. Lee, T.B., et al., *Recommended practices for surveillance: Association for Professionals in Infection Control and Epidemiology (APIC), Inc.* Am J Infect Control, 2007. **35**(7): p. 427-40.

76. Apisarnthanarak, A., et al., *Infection Prevention and Control in Asia: Current Evidence and Future Milestones.* Clin Infect Dis, 2017. **64**(suppl_2): p. S49-S50.

77. Stewardson, A., et al., *Back to the future: rising to the Semmelweis challenge in hand hygiene.* Future Microbiol, 2011. **6**(8): p. 855-76.

78. *World Health Organization.WHO Guidelines on Hand Hygiene in Health Care: a Summary [Online]. Available: http://www.who.int/gpsc/5may/tools/who_guidelines-handhygiene_summary.pdf. Accessed 7 Nov 2016.*

79. *World Health Organization. Evidence of hand hygiene to reduce transmission and infections by multidrug*

resistant organisms in health-care settings[Online]. Available:

http://www.who.int/gpsc/5may/MDRO_literature-review.pdf. Accessed 7 Nov 2016.

80. Reilly, J.S., et al., *A Pragmatic Randomized Controlled Trial of 6-Step vs 3-Step Hand Hygiene Technique in Acute Hospital Care in the United Kingdom.* Infect Control Hosp Epidemiol, 2016. **37**(6): p. 661-6.

81. Graves, N., et al., *Linking scientific evidence and decision making: a case study of hand hygiene interventions.* Infect Control Hosp Epidemiol, 2013. **34**(4): p. 424-9.

82. Luangasanatip, N., et al., *Comparative efficacy of interventions to promote hand hygiene in hospital: systematic review and network meta-analysis.* BMJ, 2015. **351**: p. h3728.

83. Hugonnet, S. and D. Pittet, *Hand hygiene-beliefs or science?* Clin Microbiol Infect, 2000. **6**(7): p. 350-6.

84. Paotong, D., et al., *Compliance with handwashing in a university hospital in Thailand.* Am J Infect Control, 2003. **31**(2): p. 128.

85. Patarakul, K., et al., *Cross-sectional survey of hand-hygiene compliance and attitudes of health care workers and visitors in the intensive care units at King Chulalongkorn Memorial Hospital.* J Med Assoc Thai, 2005. **88 Suppl 4**: p. S287-93.

86. Apisarnthanarak, A., T. Eiamsitrakoon, and L.M. Mundy, *Behavior-based interventions to improve hand hygiene adherence among intensive care unit healthcare workers in Thailand.* Infect Control Hosp Epidemiol, 2015. **36**(5): p. 517-21.

87. Pittet, D. and J.M. Boyce, *Hand hygiene and patient care: pursuing the Semmelweis legacy.* The Lancet Infectious Diseases. **1**: p. 9-20.

88. Cane, J., D. O'Connor, and S. Michie, *Validation of the theoretical domains framework for use in behaviour change and implementation research.* Implement Sci, 2012. **7**: p. 37.

89. *World Health Organization. WHO Guidelines on Hand Hygiene in Health Care: First Global Patient Safety Challenge Clean Care Is Safer Care.* 2009.

90. Whitby, M., et al., *Behavioural considerations for hand hygiene practices: the basic building blocks.* Journal of Hospital Infection, 2007. **65**(1): p. 1-8.

91. Michie, S., L. Atkins, and R. West, *The Behaviour Change Wheel A Guide To Designing Interventions.* 2014.

92. Lipworth, W., N. Taylor, and J. Braithwaite, *Can the theoretical domains framework account for the implementation of clinical quality interventions?* BMC Health Serv Res, 2013. **13**: p. 530.

93. Lawton, R., et al., *Using the Theoretical Domains Framework (TDF) to understand adherence to multiple evidence-based indicators in primary care: a qualitative study.* Implement Sci, 2016. **11**: p. 113.

94. French, S.D., et al., *Developing theory-informed behaviour change interventions to implement evidence into practice: a systematic approach using the Theoretical Domains Framework.* Implementation Science, 2012. **7**(1): p. 38.

95. Craig, P., et al., *Developing and evaluating complex interventions: the new Medical Research Council guidance.* BMJ : British Medical Journal, 2008. **337**: p. a1655.

96. White, K.M., et al., *Using a theory of planned behaviour framework to explore hand hygiene beliefs at the '5 critical moments' among Australian hospital-based nurses.* BMC health services research, 2015. **15**(1): p. 59.

97. Boscart, V.M., et al., *Using psychological theory to inform methods to optimize the implementation of a hand hygiene intervention.* Implementation Science : IS, 2012. **7**: p. 77-77.

98. Squires, J.E., et al., *Understanding practice: factors that influence physician hand hygiene compliance.* Infect Control Hosp Epidemiol, 2014. **35**(12): p. 1511-20.

99. Fuller, C., et al., *Application of a theoretical framework for behavior change to hospital workers' real-time explanations for noncompliance with hand hygiene guidelines.* Am J Infect Control, 2014. **42**(2): p. 106-10.

100. Huis, A., et al., *A systematic review of hand hygiene improvement strategies: a behavioural approach.* Implement Sci, 2012. **7**: p. 92.

101. McAteer, J., et al., *Using psychological theory to understand the challenges facing staff delivering a ward-led intervention to increase hand hygiene behavior: A qualitative study.* American Journal of Infection Control, 2014. **42**(5): p. 495-499.

102. Sax, H., et al., *The World Health Organization hand hygiene observation method.* American Journal of Infection Control, 2009. **37**(10): p. 827-834.

103. Gould, D.J., et al., *Interventions to improve hand hygiene compliance in patient care.* Cochrane Database Syst Rev, 2010(9): p. CD005186.

104. Hussey, M.A. and J.P. Hughes, *Design and analysis of stepped wedge cluster randomized trials.* Contemporary Clinical Trials, 2007. **28**(2): p. 182-191.

105. Hemming, K., et al., *The stepped wedge cluster randomised trial: rationale, design, analysis, and reporting.* BMJ, 2015. **350**: p. h391.

106. Brown, C.A. and R.J. Lilford, *The stepped wedge trial design: a systematic review.* BMC Med Res Methodol, 2006. **6**: p. 54.

107. Grayling, M.J., J.M. Wason, and A.P. Mander, *Stepped wedge cluster randomized controlled trial designs: a review of reporting quality and design features.* Trials, 2017. **18**(1): p. 33.

108. Fuller, C., et al., *The Feedback Intervention Trial (FIT)--improving hand-hygiene compliance in UK healthcare workers: a stepped wedge cluster randomised controlled trial.* PLoS One, 2012. **7**(10): p. e41617.

109. Wenzel, R.P. and M.B. Edmond, *The impact of hospital-acquired bloodstream infections.* Emerg Infect Dis, 2001. **7**(2): p. 174-7.

110. Vrijens, F., et al., *Hospital-acquired, laboratory-confirmed bloodstream infections: linking national surveillance data to clinical and financial hospital data to estimate increased length of stay and healthcare costs.* J Hosp Infect, 2010. **75**(3): p. 158-62.

111. Aiken, A.M., et al., *Risk and causes of paediatric hospital-acquired bacteraemia in Kilifi District Hospital, Kenya: a prospective cohort study.* Lancet, 2011. **378**(9808): p. 2021-7.

112. Askarian, M., H. Mahmoudi, and O. Assadian, *Incidence of Nosocomial Infections in a Big University Affiliated Hospital in Shiraz, Iran: A Six-month Experience.* Int J Prev Med, 2013. **4**(3): p. 366-72.

113. Kanoksil, M., et al., *Epidemiology, microbiology and mortality associated with community-acquired bacteremia in northeast Thailand: a multicenter surveillance study.* PLoS One, 2013. **8**(1): p. e54714.

114. Opartkiattikul, N. and S. Bejrachandra, *The external quality assessment schemes in Thailand.* Rinsho Byori, 2002. **50**(2): p. 121-5.

115. Rodriguez-Bano, J., et al., *Epidemiology and clinical features of community-acquired, healthcare-associated and nosocomial bloodstream infections in tertiary-care and community hospitals.* Clin Microbiol Infect, 2010. **16**(9): p. 1408-13.

116. Hall, K.K. and J.A. Lyman, *Updated review of blood culture contamination.* Clin Microbiol Rev, 2006. **19**(4): p. 788-802.

117. Wiersinga, W.J., B.J. Currie, and S.J. Peacock, *Melioidosis.* N Engl J Med, 2012. **367**(11): p. 1035-44.

118. *Epidemiology BO, Annual Epidemiology Surveillance Report 2010.* 2011.

119. Fortin, E., et al., *Healthcare-associated bloodstream infections secondary to a urinary focus: the Quebec provincial surveillance results.* Infect Control Hosp Epidemiol, 2012. **33**(5): p. 456-62.

120. Lee, M.C., et al., *Trends in nosocomial bloodstream infections following health care restructuring in Alberta between 1999 and 2005.* Can J Infect Dis Med Microbiol, 2010. **21**(1): p. e1-5.

121. Mitt, P., et al., *Epidemiology of nosocomial bloodstream infections in Estonia.* J Hosp Infect, 2009. **71**(4): p. 365-70.

122. Rosenthal, V.D., *Central Line-Associated Bloodstream Infections in Limited-Resource Countries: A Review of the Literature.* Clinical Infectious Diseases, 2009. **49**(12): p. 1899-1907.

123. Peleg, A.Y. and D.C. Hooper, *Hospital-acquired infections due to gram-negative bacteria.* N Engl J Med, 2010. **362**(19): p. 1804-13.

124. Pereira, C.A., et al., *Nosocomial bloodstream infections in Brazilian pediatric patients: microbiology, epidemiology, and clinical features.* PLoS One, 2013. **8**(7): p. e68144.

125. Johnson, A.P., *Methicillin-resistant Staphylococcus aureus: the European landscape.* J Antimicrob Chemother, 2011. **66 Suppl 4**: p. iv43-iv48.

126. Son, J.S., et al., *Bloodstream infections and clinical significance of healthcare-associated bacteremia: a multicenter surveillance study in Korean hospitals.* J Korean Med Sci, 2010. **25**(7): p. 992-8.

127. Rosenthal, V.D., et al., *Impact of International Nosocomial Infection Control Consortium (INICC) strategy on central line-associated bloodstream infection rates in the intensive care units of 15 developing countries.* Infect Control Hosp Epidemiol, 2010. **31**(12): p. 1264-72.

128. Rosenthal, V.D., et al., *Impact of a multidimensional infection control strategy on central line-associated bloodstream infection rates in pediatric intensive care units of five developing countries: findings of the International Nosocomial Infection Control Consortium (INICC).* Infection, 2012. **40**(4): p. 415-23.

129. Rosenthal, V.D., et al., *Findings of the International Nosocomial Infection Control Consortium (INICC), part III: effectiveness of a multidimensional infection control approach to reduce central line-associated bloodstream infections in the neonatal intensive care units of 4 developing countries.* Infect Control Hosp Epidemiol, 2013. **34**(3): p. 229-37.

130. Jaggi, N., et al., *Impact of an international nosocomial infection control consortium multidimensional approach on central line-associated bloodstream infection rates in adult intensive care units in eight cities in India.* Int J Infect Dis, 2013. **17**(12): p. e1218-24.

131. Leblebicioglu, H., et al., *Impact of a multidimensional infection control approach on central line-associated bloodstream infections rates in adult intensive care units of 8 cities of Turkey: findings of the International Nosocomial Infection Control Consortium (INICC).* Ann Clin Microbiol Antimicrob, 2013. **12**: p. 10.

132. Higuera, F., et al., *The effect of process control on the incidence of central venous catheter-associated bloodstream infections and mortality in intensive care units in Mexico.* Crit Care Med, 2005. **33**(9): p. 2022-7.

133. Rosenthal, V.D., et al., *Effect of an infection control program using education and performance feedback on rates of intravascular device-associated bloodstream infections in intensive care units in Argentina.* Am J Infect Control, 2003. **31**(7): p. 405-9.

134. Klevens, R.M., et al., *Estimating health care-associated infections and deaths in U.S. hospitals, 2002.* Public Health Rep, 2007. **122**(2): p. 160-6.

135. Cheng, A.C., et al., *Strategies to reduce mortality from bacterial sepsis in adults in developing countries.* PLoS Med, 2008. **5**(8): p. e175.

136. Duenas, L., et al., *Device-associated infections rates in pediatrics and neonatal intensive care units in El Salvador: findings of the INICC.* J Infect Dev Ctries, 2011. **5**(6): p. 445-51.

137. Guanche-Garcell, H., et al., *Device-associated infection rates in adult intensive care units of Cuban university hospitals: International Nosocomial Infection Control Consortium (INICC) findings.* Int J Infect Dis, 2011. **15**(5): p. e357-62.

138. Hu, B., et al., *Device-associated infection rates, device use, length of stay, and mortality in intensive care units of 4 Chinese hospitals: International Nosocomial Control Consortium findings.* Am J Infect Control, 2013. **41**(4): p. 301-6.

139. Kubler, A., et al., *Device-associated infection rates and extra length of stay in an intensive care unit of a university hospital in Wroclaw, Poland: International Nosocomial Infection Control Consortium's (INICC) findings.* J Crit Care, 2012. **27**(1): p. 105 e5-10.

140. Navoa-Ng, J.A., et al., *Device-associated infections rates in adult, pediatric, and neonatal intensive care units of hospitals in the Philippines: International Nosocomial Infection Control Consortium (INICC) findings.* Am J Infect Control, 2011. **39**(7): p. 548-54.

141. Rasslan, O., et al., *Device-associated infection rates in adult and pediatric intensive care units of hospitals in Egypt. International Nosocomial Infection Control Consortium (INICC) findings.* J Infect Public Health, 2012. **5**(6): p. 394-402.

142. Tao, L., et al., *Device-associated infection rates in 398 intensive care units in Shanghai, China: International Nosocomial Infection Control Consortium (INICC) findings.* Int J Infect Dis, 2011. **15**(11): p. e774-80.

143. Rosenthal, V.D., S. Guzman, and P.W. Orellano, *Nosocomial infections in medical-surgical intensive care units in Argentina: attributable mortality and length of stay.* Am J Infect Control, 2003. **31**(5): p. 291-5.

144. Rosenthal, V.D., S. Guzman, and C. Crnich, *Device-associated nosocomial infection rates in intensive care units of Argentina.* Infect Control Hosp Epidemiol, 2004. **25**(3): p. 251-5.

145. Moreno, C.A., et al., *Device-associated infection rate and mortality in intensive care units of 9 Colombian hospitals: findings of the International Nosocomial Infection Control Consortium.* Infect Control Hosp Epidemiol, 2006. **27**(4): p. 349-56.

146. Ramirez Barba, E.J., et al., *Device-associated nosocomial infection rates in intensive care units in four Mexican public hospitals.* Am J Infect Control, 2006. **34**(4): p. 244-7.

147. Rosenthal, V.D., et al., *Device-associated nosocomial infections in 55 intensive care units of 8 developing countries.* Ann Intern Med, 2006. **145**(8): p. 582-91.

148. Leblebicioglu, H., et al., *Device-associated hospital-acquired infection rates in Turkish intensive care units. Findings of the International Nosocomial Infection Control Consortium (INICC).* J Hosp Infect, 2007. **65**(3): p. 251-7.

149. Mehta, A., et al., *Device-associated nosocomial infection rates in intensive care units of seven Indian cities. Findings of the International Nosocomial Infection Control Consortium (INICC).* J Hosp Infect, 2007. **67**(2): p. 168-74.

150. Cuellar, L.E., et al., *Device-associated infection rates and mortality in intensive care units of Peruvian hospitals: findings of the International Nosocomial Infection Control Consortium.* Rev Panam Salud Publica, 2008. **24**(1): p. 16-24.

151. Rosenthal, V.D., *Device-associated nosocomial infections in limited-resources countries: findings of the International Nosocomial Infection Control Consortium (INICC).* Am J Infect Control, 2008. **36**(10): p. S171 e7-12.

152. Salomao, R., et al., *Device-associated infection rates in intensive care units of Brazilian hospitals: findings of the International Nosocomial Infection Control Consortium.* Rev Panam Salud Publica, 2008. **24**(3): p. 195-202.

153. Madani, N., et al., *Health-care associated infections rates, length of stay, and bacterial resistance in an intensive care unit of Morocco: findings of the International Nosocomial Infection Control Consortium (INICC).* Int Arch Med, 2009. **2**(1): p. 29.

154. Friedman, C., et al., *Process surveillance: auditing infection control policies and procedures.* Am J Infect Control, 1984. **12**(4): p. 228-32.

155. Baker, O.G., *Process surveillance: an epidemiologic challenge for all health care organizations.* Am J Infect Control, 1997. **25**(2): p. 96-101.

156. Higuera, F., et al., *Attributable cost and length of stay for patients with central venous catheter-associated bloodstream infection in Mexico City intensive care units: a prospective, matched analysis.* Infect Control Hosp Epidemiol, 2007. **28**(1): p. 31-5.

157. Rosenthal, V.D., et al., *The attributable cost, length of hospital stay, and mortality of central line-associated bloodstream infection in intensive care departments in Argentina: A prospective, matched analysis.* Am J Infect Control, 2003. **31**(8): p. 475-80.

158. Larson, E., *A causal link between handwashing and risk of infection? Examination of the evidence.* Infect Control, 1988. **9**(1): p. 28-36.

159. Ling, M.L., A. Apisarnthanarak, and G. Madriaga, *The Burden of Healthcare-Associated Infections in Southeast Asia: A Systematic Literature Review and Meta-analysis.* Clin Infect Dis, 2015. **60**(11): p. 1690-9.

160. Hongsuwan, M., et al., *Increasing incidence of hospital-acquired and healthcare-associated bacteremia in northeast Thailand: a multicenter surveillance study.* PLoS One, 2014. **9**(10): p. e109324.

161. Erasmus, V., et al., *Systematic review of studies on compliance with hand hygiene guidelines in hospital care.* Infect Control Hosp Epidemiol, 2010. **31**(3): p. 283-94.

162. Korniewicz, D.M. and M. El-Masri, *Exploring the factors associated with hand hygiene compliance of nurses during routine clinical practice.* Applied Nursing Research, 2010. **23**(2): p. 86-90.

163. Lee, S.S., et al., *Improved Hand Hygiene Compliance is Associated with the Change of Perception toward Hand Hygiene among Medical Personnel.* Infection & Chemotherapy, 2014. **46**(3): p. 165-171.

164. Mathai, E., et al., *Promoting hand hygiene in healthcare through national/subnational campaigns.* J Hosp Infect, 2011. **77**(4): p. 294-8.

165. Unahalekhaka, A., *Status of multidrug resistant organism transmission prevention in hospitals in Thailand.* Journal of Patient Safety & Infection Control, 2015. **3**(2): p. 44.

166. Apisarnthanarak, A., et al., *A Multifaceted Intervention to Reduce Pandrug-Resistant Acinetobacter baumannii Colonization and Infection in 3 Intensive Care Units in a Thai Tertiary Care Center: A 3-Year Study.* Clinical Infectious Diseases, 2008. **47**(6): p. 760-767.

167. Eiamsitrakoon, T., et al., *Hand hygiene behavior: translating behavioral research into infection control practice.* Infect Control Hosp Epidemiol, 2013. **34**(11): p. 1137-45.

168. Apisarnthanarak, A., et al., *Effectiveness of an Educational Program to Reduce Ventilator-Associated Pneumonia in a Tertiary Care Center in Thailand: A 4-Year Study.* Clinical Infectious Diseases, 2007. **45**(6): p. 704-711.

169. Godin, G., et al., *Healthcare professionals' intentions and behaviours: A systematic review of studies based on social cognitive theories.* Implementation Science : IS, 2008. **3**: p. 36-36.

170. McHugh, M.L., *Interrater reliability: the kappa statistic.* Biochemia Medica, 2012. **22**(3): p. 276-282.

171. Bland, J.M. and D.G. Altman, *Statistics notes: Cronbach's alpha.* BMJ, 1997. **314**(7080): p. 572.

172. Mukaka, M.M., *A guide to appropriate use of Correlation coefficient in medical research.* Malawi Medical Journal : The Journal of Medical Association of Malawi, 2012. **24**(3): p. 69-71.

173. Zhang, Y. and B. Wildemuth, *Qualitative Analysis of Content [w:] Applications of Social Research Methods to Questions in Information and Library Science, red.* Barbara M. Wildemuth,.(West Port, Connecticut: Libraries Unlimited, 2009), 2009. **308**.

174. Dyson, J., et al., *Development of a theory-based instrument to identify barriers and levers to best hand hygiene practice among healthcare practitioners.* Implement Sci, 2013. **8**: p. 111.

175. Gould, D. and A. Chamberlain, *The use of a ward-based educational teaching package to enhance nurses' compliance with infection control procedures.* Journal of Clinical Nursing, 1997. **6**(1): p. 55-67.

176. Abraham, C. and S. Michie, *A taxonomy of behavior change techniques used in interventions.* Health Psychol, 2008. **27**(3): p. 379.

177. Mayer, J., et al., *Dissemination and sustainability of a hospital-wide hand hygiene program emphasizing positive reinforcement.* Infect Control Hosp Epidemiol, 2011. **32**(1): p. 59-66.

178. Huang, T.T. and S.C. Wu, *Evaluation of a training programme on knowledge and compliance of nurse assistants' hand hygiene in nursing homes.* Journal of Hospital Infection, 2008. **68**(2): p. 164-170.

179. Contzen, N., S. De Pasquale, and H.J. Mosler, *Over-Reporting in Handwashing Self-Reports: Potential Explanatory Factors and Alternative Measurements.* PLoS One, 2015. **10**(8): p. e0136445.

180. Larson, E.L., A.E. Aiello, and J.P. Cimiotti, *Assessing nurses' hand hygiene practices by direct observation or self-report.* J Nurs Meas, 2004. **12**(1): p. 77-85.

181. Seyed Nematian, S.S., et al., *Comparing knowledge and self-reported hand hygiene practices with direct observation among Iranian hospital nurses.* Am J Infect Control, 2017. **45**(6): p. e65-e67.

182. Michie, S., et al., *The behavior change technique taxonomy (v1) of 93 hierarchically clustered techniques: building an international consensus for the reporting of behavior change interventions.* Ann Behav Med, 2013. **46**(1): p. 81-95.

183. Luangasanatip, N., et al., *Comparative efficacy of interventions to promote hand hygiene in hospital: systematic review and network meta-analysis.* BMJ : British Medical Journal, 2015. **351**: p. h3728.

184. Fleming, A., et al., *Antibiotic prescribing in long-term care facilities: a qualitative, multidisciplinary investigation.* BMJ Open, 2014. **4**(11): p. e006442.

185. Boscart, V.M., et al., *Using psychological theory to inform methods to optimize the implementation of a hand hygiene intervention.* Implement Sci, 2012. **7**: p. 77.

186. Steinmo, S., et al., *Characterising an implementation intervention in terms of behaviour change techniques and theory: the 'Sepsis Six' clinical care bundle.* Implement Sci, 2015. **10**: p. 111.

187. Cohen, A.L., et al., *Recommendations for metrics for multidrug-resistant organisms in healthcare settings: SHEA/HICPAC Position paper.* Infect Control Hosp Epidemiol, 2008. **29**(10): p. 901-13.

188. Larson, E., *Skin Hygiene and Infection Prevention: More of the Same or Different Approaches?* Clinical Infectious Diseases, 1999. **29**(5): p. 1287-1294.

189. Lee, Y.T., et al., *Time-series analysis of the relationship of antimicrobial use and hand hygiene promotion with the incidence of healthcare-associated infections.* J Antibiot (Tokyo), 2012. **65**(6): p. 311-6.

190. Vernaz, N., et al., *Temporal effects of antibiotic use and hand rub consumption on the incidence of MRSA and Clostridium difficile.* J Antimicrob Chemother, 2008. **62**(3): p. 601-7.

191. Thi Anh Thu, L., et al., *Cost-effectiveness of a hand hygiene program on health care-associated infections in intensive care patients at a tertiary care hospital in Vietnam.* Am J Infect Control, 2015. **43**(12): p. e93-9.

192. Mdege, N.D., et al., *Systematic review of stepped wedge cluster randomized trials shows that design is particularly used to evaluate interventions during routine implementation.* J Clin Epidemiol, 2011. **64**(9): p. 936-48.

193. Beard, E., et al., *Stepped wedge randomised controlled trials: systematic review of studies published between 2010 and 2014.* Trials, 2015. **16**: p. 353.

194. Eckmanns, T., et al., *Compliance with antiseptic hand rub use in intensive care units: the Hawthorne effect.* Infect Control Hosp Epidemiol, 2006. **27**(9): p. 931-4.

195. McAteer, J., et al., *Development of an observational measure of healthcare worker hand-hygiene behaviour: the hand-hygiene observation tool (HHOT).* Journal of Hospital Infection, 2008. **68**(3): p. 222-229.

196. Huis, A., et al., *Impact of a team and leaders-directed strategy to improve nurses' adherence to hand hygiene guidelines: a cluster randomised trial.* Int J Nurs Stud, 2013. **50**(4): p. 464-74.

197. Arntz, P.R., et al., *Effectiveness of a multimodal hand hygiene improvement strategy in the emergency department.* Am J Infect Control, 2016. **44**(11): p. 1203-1207.

198. Chen, J.K., et al., *Impact of implementation of the World Health Organization multimodal hand hygiene improvement strategy in a teaching hospital in Taiwan.* Am J Infect Control, 2016. **44**(2): p. 222-7.

199. Haley, R.W., et al., *Study on the efficacy of nosocomial infection control (SENIC Project): summary of study design.* American Journal of Epidemiology, 1980. **111**.

200. Stone, P.W., et al., *State of infection prevention in US hospitals enrolled in the National Health and Safety Network.* Am J Infect Control, 2014. **42**(2): p. 94-9.

201. Lim, C., et al., *Epidemiology and burden of multidrug-resistant bacterial infection in a developing country.* Elife, 2016. **5**.

202. Apisarnthanarak, A. and V.J. Fraser, *Feasibility and Efficacy of Infection-Control Interventions to Reduce the Number of Nosocomial Infections and Drug-Resistant Microorganisms in Developing Countries: What Else Do We Need?* Clinical Infectious Diseases, 2009. **48**(1): p. 22-24.

203. Apisarnthanarak, A., et al., *National survey of practices to prevent healthcare-associated infections in Thailand: the role of safety culture and collaboratives.* Infect Control Hosp Epidemiol, 2012. **33**(7): p. 711-7.

204. Griffiths, P., et al., *Impact of organisation and management factors on infection control in hospitals: a scoping review.* Journal of Hospital Infection, 2009. **73**(1): p. 1-14.

205. Erasmus, V., et al., *The ACCOMPLISH study. A cluster randomised trial on the cost-effectiveness of a multicomponent intervention to improve hand hygiene compliance and reduce healthcare associated infections.* BMC Public Health, 2011. **11**: p. 721.

206. Stewardson, A.J., et al., *Enhanced performance feedback and patient participation to improve hand hygiene compliance of health-care workers in the setting of established multimodal promotion: a single-centre, cluster randomised controlled trial.* Lancet Infect Dis, 2016. **16**(12): p. 1345-1355.

207. Sikkens, J.J., et al., *Behavioral Approach to Appropriate Antimicrobial Prescribing in Hospitals: The Dutch Unique Method for Antimicrobial Stewardship (DUMAS) Participatory Intervention Study.* JAMA Intern Med, 2017. **177**(8): p. 1130-1138.

Appendices

Appendix A

Chapter 2 Supplementary

A.1: Factors influencing adherence to recommended hand hygiene practices reported by the WHO Guidelines on Hand Hygiene in Health Care[78]

Observed risk factors for poor adherence to recommended hand hygiene practices
Doctor status (rather than a nurse)
Nursing assistant status (rather than a nurse)
Physiotherapist
Technician
Male gender
Working in intensive care
Working in surgical care unit
Working in emergency care
Working during the week (vs. week-end)
Wearing gowns/gloves
Before contact with patient environment
After contact with patient environment e.g. equipment
Caring for patients aged less than 65 years' old
Patient care in non-isolation room
Duration of contact with patient (< or equal to 2 minutes)
Interruption in patient-care activities
Automated sink
Activities with high risk of cross-transmission
Understaffing/overcrowding
High number of opportunities for hand hygiene per hour of patient care

A.1: Factors influencing adherence to recommended hand hygiene practices reported by the WHO Guidelines on Hand Hygiene in Health Care[78] (cont.)

Self-reported factors for poor adherence with hand hygiene
Handwashing agents cause irritation and dryness
Sinks are inconveniently located/shortage of sinks
Lack of soap, paper, towel
Often too busy/insufficient time
Patient needs take priority
Hand hygiene interferes with HCW-patient relation
Low risk of acquiring infection from patients
Wearing of gloves/beliefs that glove use obviates the need for hand hygiene
Lack of knowledge of guidelines/protocols
Lack of knowledge, experience and education
Lack of rewards/encouragement
Lack of role model from colleagues or superiors
Not thinking about it/forgetfulness
Scepticism about the value of hand hygiene
Disagreement with the recommendations
Lack of scientific information of definitive impact of improved hand hygiene on HCAI
Additional perceived barriers to appropriate hand hygiene
Lack of active participation in hand hygiene promotion at individual or institutional level
Lack of institutional priority for hand hygiene
Lack of administrative sanction of non-compliers/rewarding of compliers
Lack of institutional safety climate/culture of personal accountability of HCWs to perform hand hygiene

Appendix B

Chapter 3 Supplementary

อนุมัติ
1 5 พ.ย. 2554

คณะกรรมการจริยธรรมการวิจัยในมนุษย์
สถาบันพัฒนาการคุ้มครองการวิจัยในมนุษย์ (สคม.)

เอกสารโครงการวิจัย
เรื่อง

"โครงการวิจัยแบบย้อนหลังและตัดขวาง เพื่อศึกษาถึงอุบัติการณ์ และอัตราการเสียชีวิตที่แท้จริงจากโรคติดเชื้อแบคทีเรียในภาคตะวันออกเฉียงเหนือของประเทศไทย"

"A retrospective cross-sectional study to define the true incidence and mortality rate of bacterial infection in northeast of Thailand"

เสนอเพื่อขอรับการพิจารณาจาก

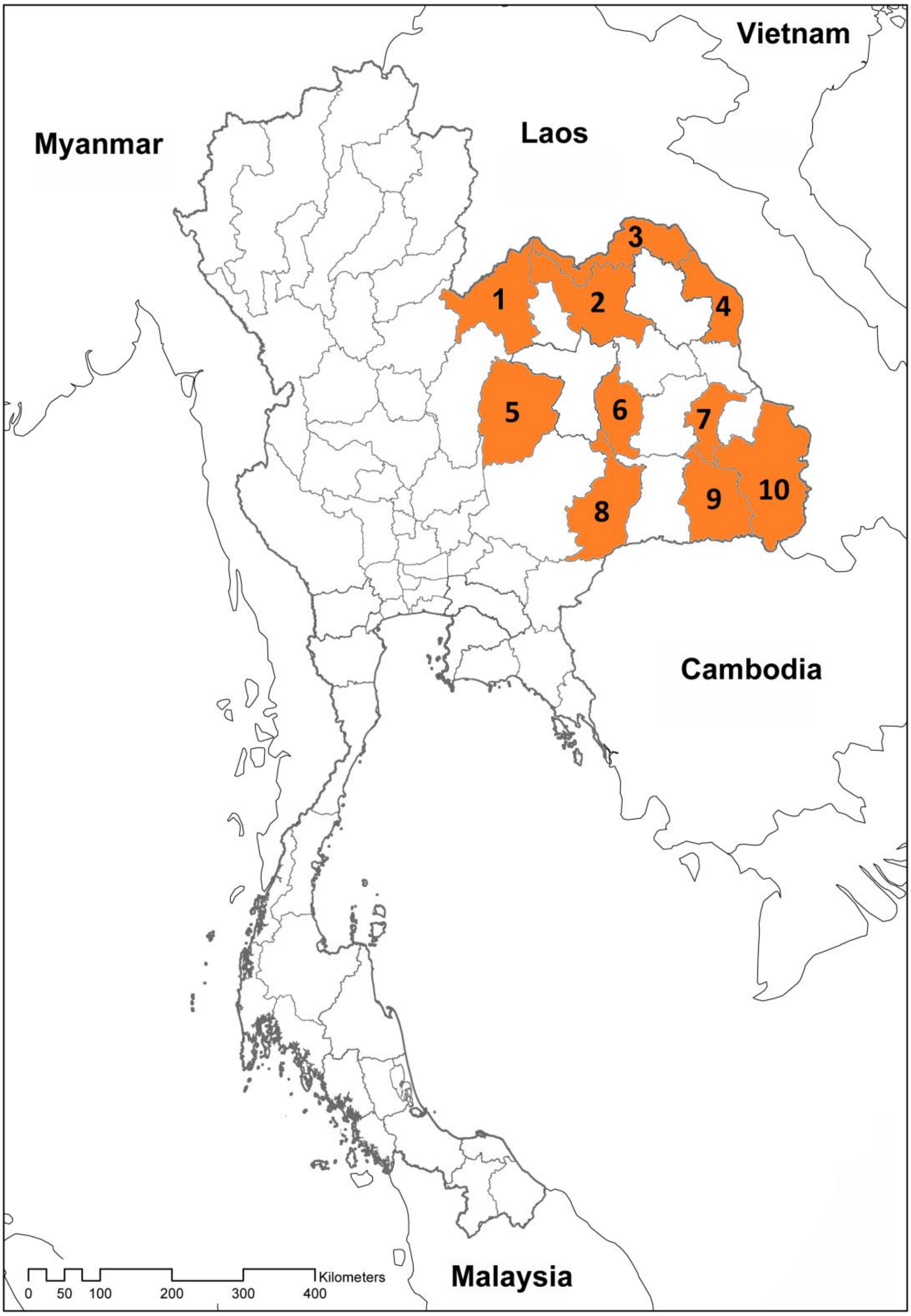
คณะกรรมการจริยธรรมการวิจัยในมนุษย์
สถาบันพัฒนาการคุ้มครองการวิจัยในมนุษย์

B.2: List of participating hospitals

Names of participating hospitals	Directors of the hospitals
1. Buriram hospital	Chalit Thongprayoon
2. Chaiyaphum hospital	Sompong Charoenwat
3. Loei hospital	Pramoth Boonjian
4. Mahasarakham hospital	Sunthorn Yontrakul
5. Nakhon Phanom hospital	Somkid Suriyalert
6. Nong Khai hospital	Kittisak Danwiboon
7. Sisaket hospital	Udom Petpuwadee
8. Ubon Ratchathani hospital	Manas Kanoksil
9. Udon Thani hospital	Pichart Dolchalermyuttana
10. Yasothorn hospital	Charan Thongthap

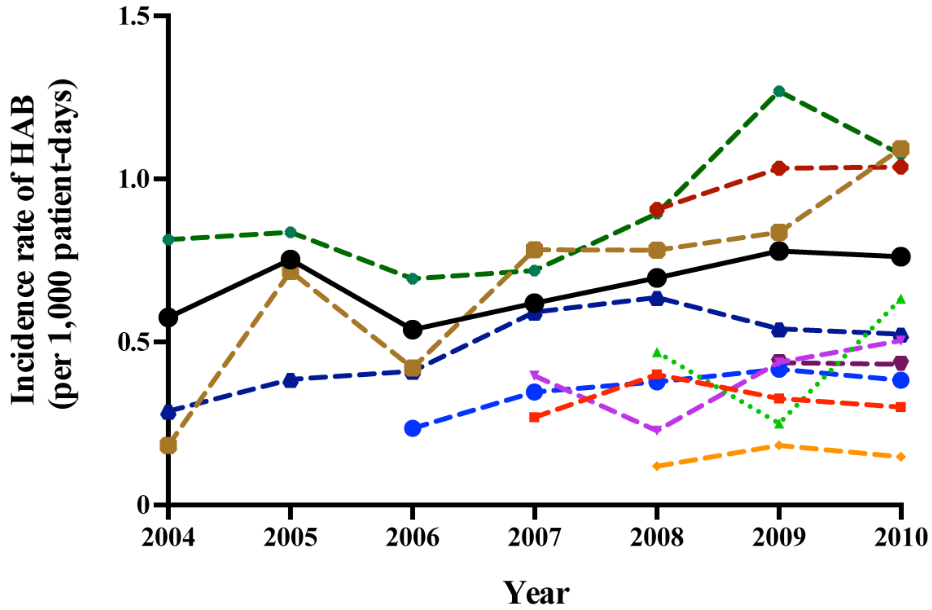
B.3: Location of participating hospitals

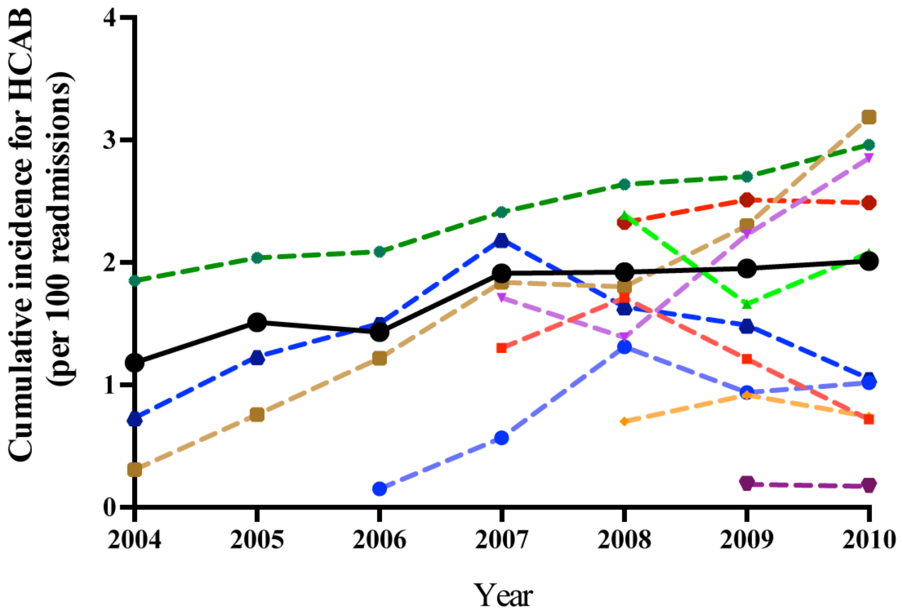
These were situated in: (1) Loei, (2) Udon Thani, (3) Nong Khai, (4) Nakhon Phanom, (5) Chaiyaphum, (6) Mahasarakarm, (7) Yasothorn, (8) Buriram, (9) Sisaket, and (10) Ubon Ratchathani



Vietnam
Laos
Myanmar
1
2
3
4
5
6
7
8
9
10
Cambodia
Malaysia
0 50 100 200 300 400
Kilometers

B.4: Trend in hospital-acquired bacteraemia (HAB) (top panel) and healthcare-associated bacteraemia (HCAB) (bottom panel) in ten provincial hospitals in Thailand





B.5: Top five most common isolates causing primary episode of hospital-acquired bacteraemia (HAB) and healthcare-associated bacteraemia (HCAB) by year in northeast Thailand between 2004 and 2010

Year	HAB	HCAB
2004 (%)	*Acinetobacter* spp (20.3%)	*Escherichia coli* (27.9%)
	Escherichia coli (14.2%)	*Staphylococcus aureus* (15.1%)
	Klebsiella pneumoniae (12.3%)	*Pseudomonas* spp (12.8%)
	Staphylococcus aureus (12.3%)	*Klebsiella pneumoniae* (9.3%)
	Enterobacter spp (8.5%)	*Acinetobacter* spp (5.8%)
2005 (%)	*Pseudomonas* spp (14.0%)	*Escherichia coli* (24.0%)
	Acinetobacter spp (13.4%)	*Pseudomonas* spp (20.8%)
	Staphylococcus aureus (12.0%)	*Staphylococcus aureus* (14.4%)
	Escherichia coli (11.6%)	*Klebsiella pneumoniae* (8.8%)
	Klebsiella spp (11.3%)	*Klebsiella* spp (4.8%)
2006 (%)	*Acinetobacter* spp (15.1%)	*Escherichia coli* (27.4%)
	Staphylococcus aureus (14.7%)	*Staphylococcus aureus* (13.4%)
	Klebsiella pneumoniae (14.3%)	*Pseudomonas* spp (10.8%)
	Escherichia coli (12.0%)	Non-typhoidal *Salmonella* (8.9%)
	Pseudomonas spp (10.4%)	*Klebsiella pneumoniae* (6.4%)
2007 (%)	*Acinetobacter* spp (13.1%)	*Escherichia coli* (24.3%)
	Staphylococcus aureus(12.8%)	*Staphylococcus aureus* (12.5%)
	Pseudomonas spp (12.6%)	*Klebsiella pneumoniae* (9.6%)
	Escherichia coli (11.8%)	Polymicrobial infections (8.1%)
	Klebsiella pneumoniae (11.8%)	*Pseudomonas* spp (7.7%)

B.5: Top five most common isolates causing primary episode of hospital-acquired bacteraemia (HAB) and healthcare-associated bacteraemia (HCAB) by year in northeast Thailand between 2004 and 2010 (cont.)

Year	HAB	HCAB
2008 (%)	*Klebsiella pneumoniae* (17.3%)	*Escherichia coli* (27.6%)
	Acinetobacter spp (15.6%)	Staphylococcus aureus (18.9%)
	Staphylococcus aureus (15.2%)	*Klebsiella pneumoniae* (11.7%)
	Escherichia coli (14.4%)	Non-typhoidal *Salmonella* (6.0%)
	Pseudomonas spp (8.6%)	*Pseudomonas* spp (6.0%)
2009 (%)	*Acinetobacter* spp (19.4%)	*Escherichia coli* (27.7%)
	Staphylococcus aureus (14.8%)	*Staphylococcus aureus* (16.1%)
	Klebsiella pneumoniae (13.2%)	*Klebsiella pneumoniae* (7.8%)
	Escherichia coli (12.5%)	*Pseudomonas* spp (7.4%)
	Pseudomonas spp (8.7%)	*Acinetobacter* spp (5.9%)
2010 (%)	*Acinetobacter* spp (15.0%)	*Escherichia coli* (25.1%)
	Klebsiella pneumoniae (14.6%)	*Staphylococcus aureus* (13.4%)
	Staphylococcus aureus (13.4%)	*Pseudomonas* spp (11.2%)
	Pseudomonas spp (12.3%)	*Klebsiella pneumoniae* (11.0%)
	Escherichia coli (12.2%)	*Acinetobacter* spp (6.4%)

B.6: Top five most common isolates causing primary episode of hospital-acquired bacteraemia (HAB) and of healthcare-associated bacteraemia (HCAB) by provincial hospital in northeast Thailand between 2004 and 2010

Hospital	HAB	HCAB
Hospital A (%)	*Staphylococcus aureus* (19.3%)	*Escherichia coli* (29.7%)
	Acinetobacter spp (17.5%)	*Klebsiella pneumoniae* (12.5%)
	Pseudomonas spp (14.0%)	*Pseudomonas* spp (9.4%)
	Escherichia coli (8.8%)	Polymicrobial infections (7.8%)
	Klebsiella pneumoniae (5.3%)	Other Gram negatives (6.3%)
Hospital B (%)	*Staphylococcus aureus* (20.0%)	*Escherichia coli* (28.7%)
	Acinetobacter spp (15.0%)	*Staphylococcus aureus* (21.8%)
	Enterococcus spp (15.0%)	*Klebsiella pneumoniae* (8.1%)
	Escherichia coli (11.3%)	*Pseudomonas* spp (8.1%)
	Klebsiella pneumoniae (8.8%)	*Enterococcus* spp (6.9%)
Hospital C (%)	*Escherichia coli* (14.8%)	*Escherichia coli* (28.8%)
	Unspecified Gram positives (12.4%)	Unspecified Gram positives (15.6%)
	Klebsiella pneumoniae (9.9%)	*Klebsiella pneumoniae* (10.2%)
	Acinetobacter spp (7.4%)	Polymicrobial infections (9.3%)
	Group D streptococcus (7.4%)	*Staphylococcus aureus* (7.6%)
Hospital D (%)	*Staphylococcus aureus* (16.7%)	*Escherichia coli* (32.7%)
	Candida spp (16.7%)	*Staphylococcus aureus* (23.1%)
	Pseudomonas spp (12.5%)	*Klebsiella* spp (11.5%)
	Escherichia coli (8.3%)	Non-typhoidal *Salmonella* (9.6%)
	Klebsiella spp (8.3%)	*Streptococcus pneumoniae* (7.7%)

B.6: Top five most common isolates causing primary episode of hospital-acquired bacteraemia (HAB) and of healthcare-associated bacteraemia (HCAB) by provincial hospital in northeast Thailand between 2004 and 2010 (cont.)

Hospital	HAB	HCAB
Hospital E (%)	*Acinetobacter* spp (22.2%)	*Escherichia coli* (36.4%)
	Unspecified Gram positives (13.9%)	Unspecified Gram positives (18.2%)
	Staphylococcus aureus (12.0%)	*Enterobacter* spp (9.1%)
	Pseudomonas spp (9.3%)	*Staphylococcus aureus* (7.8%)
	Escherichia coli (8.3%)	*Klebsiella pneumoniae* (5.2%)
Hospital F (%)	*Pseudomonas* spp (18.6%)	*Escherichia coli* (27.1%)
	Escherichia coli (17.1%)	*Staphylococcus aureus* (16.0%)
	Staphylococcus aureus (12.6%)	*Pseudomonas* spp (15.7%)
	Acinetobacter spp (11.8%)	*Klebsiella pneumoniae* (8.5%)
	Klebsiella spp (10.6%)	*Klebsiella* spp (6.1%)
Hospital G (%)	*Klebsiella pneumoniae* (20.7%)	*Escherichia coli* (30.0%)
	Staphylococcus aureus (16.7%)	*Staphylococcus aureus* (9.2%)
	Escherichia coli (12.6%)	Non-typhoidal *Salmonella* (8.1%)
	Acinetobacter spp (11.9%)	*Klebsiella pneumoniae* (8.1%)
	Enterococcus spp (5.6%)	*Pseudomonas* spp (6.5%)
Hospital H (%)	*Acinetobacter* spp (18.5%)	*Escherichia coli* (16.4%)
	Klebsiella pneumoniae (15.1%)	*Achromobacter* spp (14.8%)
	Escherichia coli (14.3%)	*Klebsiella pneumoniae* (13.1%)
	Staphylococcus aureus (10.1%)	*Acinetobacter* spp (13.1%)
	Enterococcus spp (9.2%)	*Staphylococcus aureus* (12.3%)

B.6: Top five most common isolates causing primary episode of hospital-acquired bacteraemia (HAB) and of healthcare-associated bacteraemia (HCAB) by provincial hospital in northeast Thailand between 2004 and 2010 (cont.)

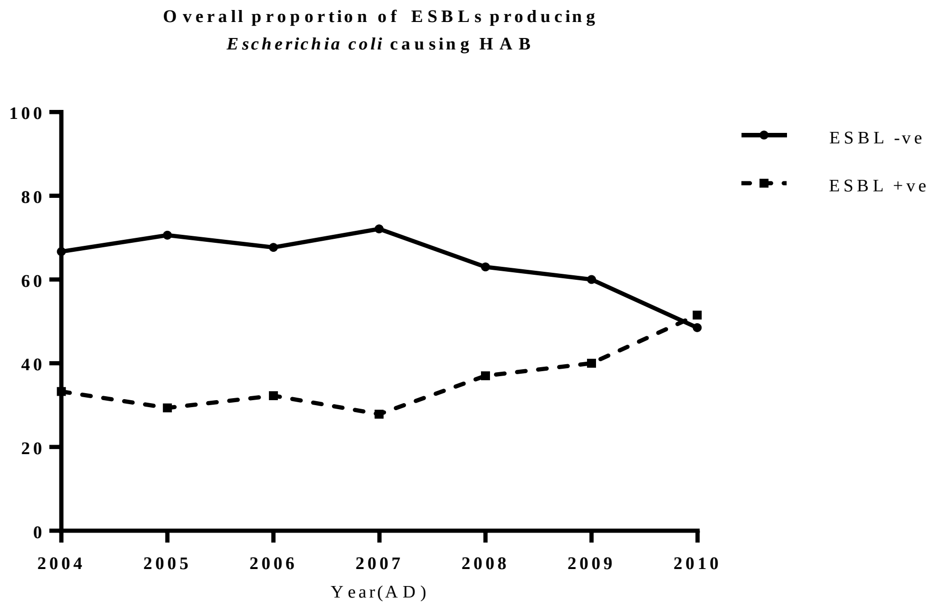
Hospital	**HAB**	**HCAB**
Hospital I (%)	*Klebsiella pneumoniae* (19.3%)	*Escherichia coli* (28.6%)
	Escherichia coli (13.7%)	*Staphylococcus aureus* (10.9%)
	Staphylococcus aureus (12.5%)	*Klebsiella pneumoniae* (10.5%)
	Acinetobacter spp (10.3%)	*Acinetobacter* spp (8.2%)
	Candida spp (8.0%)	Non-typhoidal *Salmonella* (5.6%)
Hospital J (%)	*Acinetobacter* spp (20.3%)	*Escherichia coli* (23.3%)
	Staphylococcus aureus (14.6%)	*Staphylococcus aureus* (16.9%)
	Klebsiella pneumoniae (13.5%)	*Pseudomonas* spp (12.2%)
	Pseudomonas spp (11.2%)	*Klebsiella pneumoniae* (10.6%)
	Escherichia coli (11.4%)	Non-typhoidal *Salmonella* (6.4%)

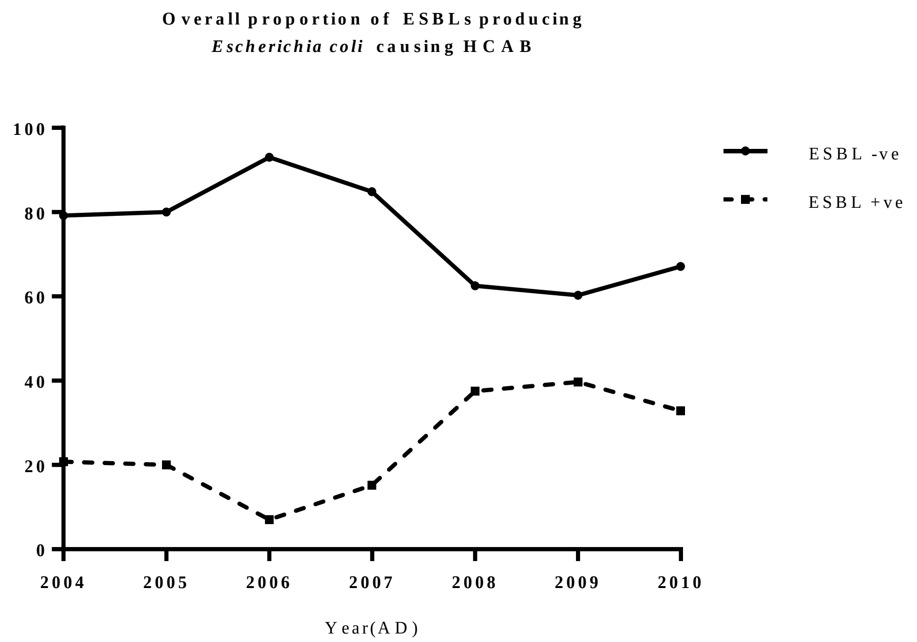
B.7: Proportions of ESBL-producing *E. coli,* ESBL-producing *K. pneumoniae,* and MRSA as a cause of hospital-acquired bacteraemia (HAB) over time in northeast Thailand

Year	ESBL-producing *E. coli*	ESBL-producing *K. pneumoniae*	MRSA
2004	10/30 (33.3%)	19/26 (73.1%)	14/26 (53.9%)
2005	10/34 (29.4%)	20/30 (66.7%)	21/35 (60.0%)
2006	10/31 (32.3%)	27/37 (73.0%)	15/38 (39.5%)
2007	12/43 (27.9%)	30/43 (69.8%)	16/47 (34.0%)
2008	34/92 (37.0%)	69/111 (62.2%)	32/97 (33.3%)
2009	42/105 (40.0%)	51/111 (46.0%)	34/124 (27.4%)
2010	51/99 (51.5%)	67/119 (56.3%)	32/109 (29.4%)
Overall	169/434 (38.9%)	283/477 (59.3%)	164/476 (34.5%)
P value *	0.005	0.002	<0.001

* Chi-square test for trend

B.8: Trend in overall proportion of ESBLs producing *Escherichia coli* causing hospital-acquired bacteraemia (HAB) (left panel) and causing and healthcare-associated bacteraemia (HCAB) (right panel) in provincial hospitals in Thailand



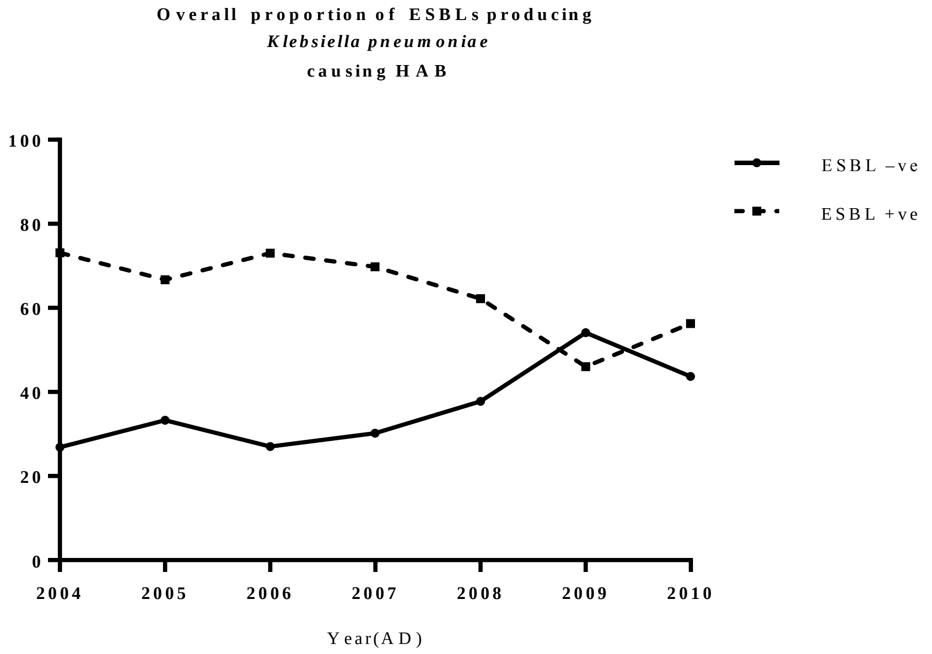


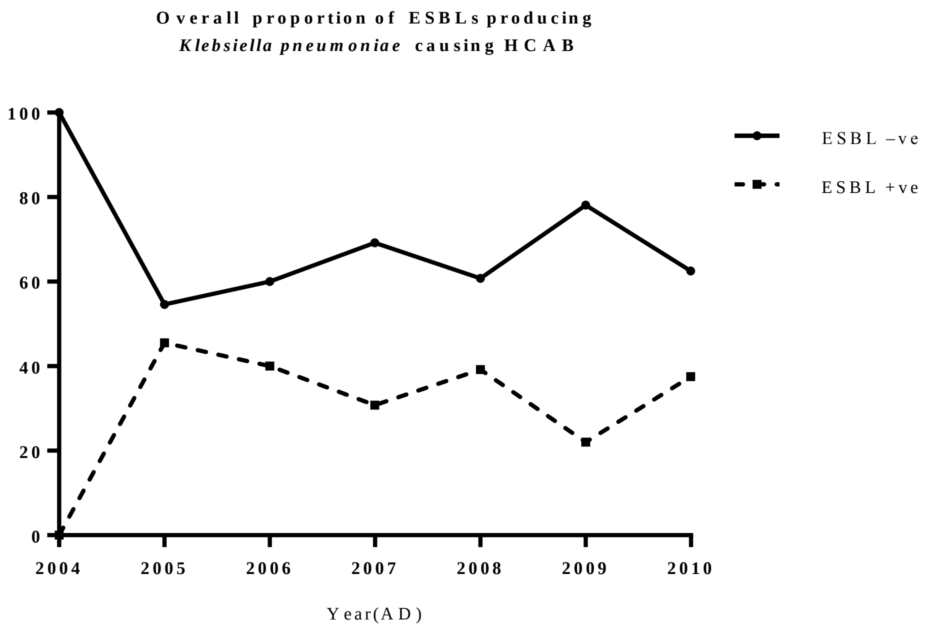
B.9: Proportions of ESBL-producing *E. coli,* ESBL-producing *K. pneumoniae,* and MRSA as a cause of healthcare-associated bacteraemia (HCAB) over time in northeast Thailand

Year	ESBL-producing *E. coli*	ESBL-producing *K. pneumoniae*	MRSA
2004	5/24 (20.8%)	0/8 (0.0%)	2/13 (15.4%)
2005	6/30 (20.0%)	5/11 (45.5%)	3/18 (16.7%)
2006	3/43 (7.0%)	4/10 (40.0%)	8/21 (38.1%)
2007	10/66 (15.2%)	8/26 (30.8%)	5/34 (14.7%)
2008	45/120 (37.5%)	20/51 (39.2%)	8/56 (14.3%)
2009	58/146 (39.7%)	9/41 (22.0%)	20/85 (23.5%)
2010	48/146 (32.9%)	24/64 (37.5%)	21/78 (26.9%)
Overall	175/575 (30.4%)	70/211 (33.2%)	67/305 (22.0%)
P value *	<0.001	0.557	0.383

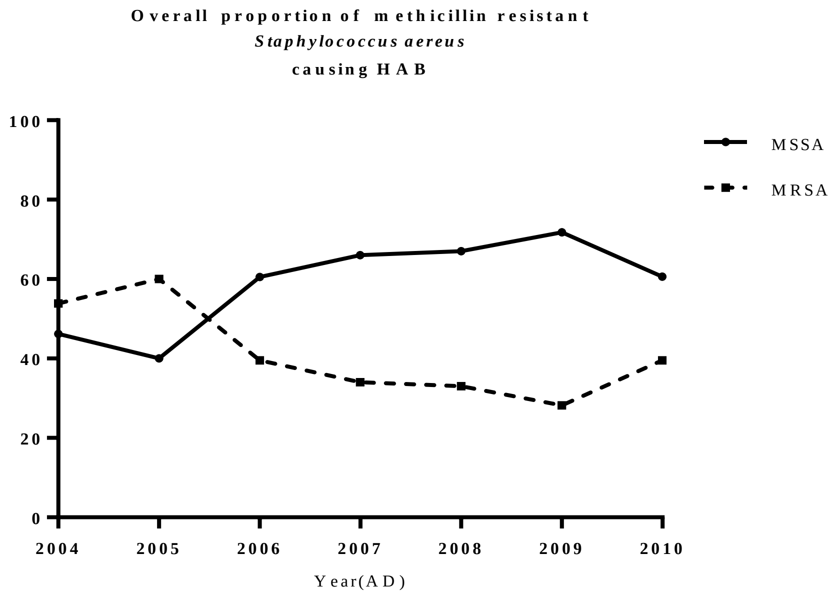
* Chi-square test for trend

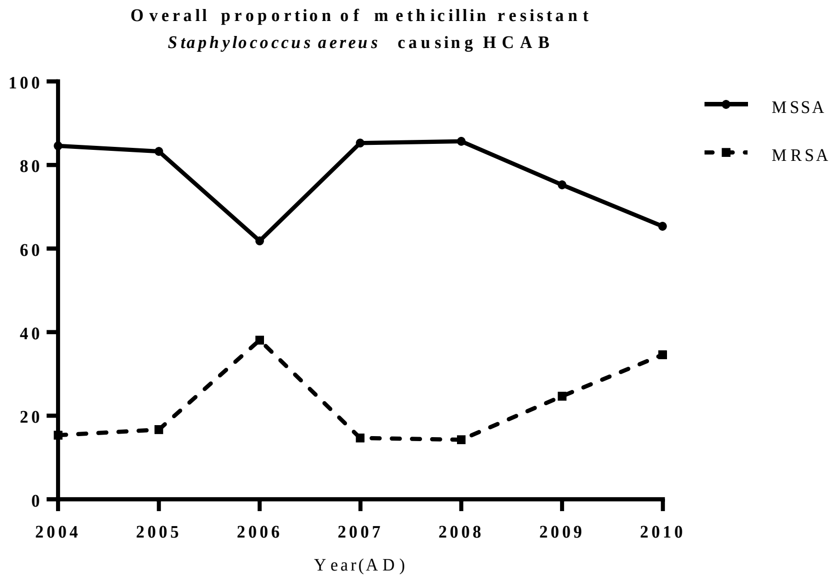
B.10: Trend in overall proportion of ESBLs producing *Klebsiella pneumonia* causing hospital-acquired bacteraemia (HAB) (left panel) and causing and healthcare-associated bacteraemia (HCAB) (right panel) in provincial hospitals in Thailand





B.11: Trend in overall proportion of methicillin resistant *Staphylococcus aureus* causing hospital-acquired bacteraemia (HAB) (left panel) and causing and healthcare-associated bacteraemia (HCAB) (right panel) in provincial hospitals in Thailand





Appendix C

Chapter 4 Supplementary

MUTM 2010-054-01

FACULTY OF TROPICAL MEDICINE

CERTIFICATE OF ETHICAL APPROVAL
Ethics Committee of the Faculty of Tropical Medicine, Mahidol University
420/6 Ratchawithi Rd., Ratchathewee, Bangkok 10400, Thailand

This Certificate of Ethical Approval (MUTM 2010-054-01) applies to the

Project entitled: A non-interventional investigation into infection control practices, and obstacles to improvements amongst healthcare workers at a regional hospital

EC Submission No.: TMEC 10-035

with the following relevant documents:

Research proposal:	English, version 2.0 dated 26 October 2010 (based on full protocol version 2.0 dated 26 October 2010)
Participant Information Sheet for Doctors, Nurses, Practical nurses, Nurse-aid:	Thai, version 2.0 dated 26 October 2010
Participant Information Sheet for Medical/Nurse students:	Thai, version 2.0 dated 26 October 2010
Participant Information Sheet for Management Team:	Thai, version 2.0 dated 26 October 2010
Questionnaires Form:	Thai, version 2.0 dated 26 October 2010
Semi-structured interviews Form:	Thai, version 2.0 dated 26 October 2010
Focus group Discussion Form:	Thai, version 2.0 dated 26 October 2010
Observation Form:	Thai, version 2.0 dated 26 October 2010
Ward Infrastructure Survey Form:	Thai, version 1.0 dated 13 July 2010

Oxford Tropical Research Ethics Committee

University of Oxford
Room 8, Manor House
The John Radcliffe, Headington, Oxford OX3 9DZ
tel. +44 (0) 1865 743005, fax +44 (0) 1865 743 002
e-mail: Fiona.Goulthorp@admin.ox.ac.uk

UNIVERSITY OF OXFORD

Dr D Limmathurotsakul
Department of Tropical Hygiene
Mahidol Oxford Research Unit
Faculty of Tropical Medicine
Mahidol University
Thailand

14th February 2011

Dear Dr Limmathurotsakul

Full Title of Study: A non-interventional investigation into infection control practices and obstacles to improvements amongst healthcare workers (HCWs)at a regional hospital in NE Thailand

OXTREC Reference: 08-11

The OXTREC executive team reviewed the above application

In addition to your application, the documents reviewed were:

Documentation:	**Version:**	**Date:**
Protocol	V2.0	26.10.2010
Participant Information Sheet	V2.0	26.10.2010
Participant Consent Form	V1.0	13.07.2010
LEC approval letter		09.11.2010

The executive team gave approval to the study subject to a correction of the dates of the study's duration in the participant information sheets (the translated versions give dates which we believe you have changed).

We look forward to receiving your annual/end of study report.

Yours sincerely,

Richard Mayon-White

Dr Richard Mayon-White

OXTREC Chair

C.2: Theoretical Domains Framework and example questions

Theoretical domain	Operational definition*	Sample question
TDF1: Knowledge	Knowledge of the rules, protocol or indications governing hand hygiene	Which of the following hand hygiene actions prevents transmission of germs to the health-care worker
TDF2: Skills	Necessary practical skills and competencies to perform hand hygiene	How many times on hand hygiene training
TDF3: Social/professional role and identity	A coherent set of behaviours and displayed personal qualities of an individual in a social or work setting.	You dare not remind colleagues and doctors to wash their hands. Because medical personnel and would know how to treat it.
TDF4: Beliefs about capabilities	Acceptance of the truth, reality or validity about an ability, talent or facility that a person can put to constructive use, for example, self-confidence.	Do you think washing hands immediately after nursing caused confidence in the care of other patients next
TDF5: Optimism	The confidence that things will happen for the best or that desired goals will be attained, for example, optimism, pessimism.	% of self-reported on hand hygiene

*Operation definitions are adapted from Cane *et al*., 2012

TDF = Theoretical Domains Framework

C.2: Theoretical Domains Framework and example questions

Theoretical domain	Operational definition*	Sample question
TDF1: Knowledge	Knowledge of the rules, protocol or indications governing hand hygiene	Which of the following hand hygiene actions prevents transmission of germs to the health-care worker
TDF2: Skills	Necessary practical skills and competencies to perform hand hygiene	How many times on hand hygiene training
TDF3: Social/professional role and identity	A coherent set of behaviours and displayed personal qualities of an individual in a social or work setting.	You dare not remind colleagues and doctors to wash their hands. Because medical personnel and would know how to treat it.
TDF4: Beliefs about capabilities	Acceptance of the truth, reality or validity about an ability, talent or facility that a person can put to constructive use, for example, self-confidence.	Do you think washing hands immediately after nursing caused confidence in the care of other patients next
TDF5: Optimism	The confidence that things will happen for the best or that desired goals will be attained, for example, optimism, pessimism.	% of self-reported on hand hygiene

*Operation definitions are adapted from Cane *et al*., 2012

TDF = Theoretical Domains Framework

C.2: Theoretical Domains Framework and example questions (cont.)

Theoretical domain	Operational definition*	Sample question
TDF6: Beliefs about consequences	Perceived consequences of hand hygiene, *i.e.,* what are the costs/benefits to patients and healthcare workers Cognitive evaluation of the consequences of hand hygiene, including transmission of microorganisms, control over the environment, and professional behaviour	Do you think nurse no need to perform hand washing after taking off gloves because it has no directly contact to patient
TDF7:Reinforcement	Increasing the probability of a response by arranging a dependent relationship, or contingency, between the response and a given stimulus, for example, rewards.	Opened question on list of obstacle
TDF8: Intentions	Plans to adhere to hand hygiene recommendations in a variety of clinical situations	Do you think nurses should wash their hands before and after patient care
TDF9: Goals	Mental representations of outcomes or end states that an individual wants to achieve, for example, goal/target setting.	I want all staff to wash their hands before and after nursing
TDF10: Memory, attention, and decision processes	Forgetting to perform hand hygiene, concentration on/attention to another task, i.e., being distracted by another non-urgent task, or making a conscious decision not to clean hands because another task is more urgent	Whether rush just need to wash their hands before providing nursing care

*Operation definitions are adapted from Cane *et al*., 2012

TDF = Theoretical Domains Framework

C.2: Theoretical Domains Framework and example questions (cont.)

Theoretical domain	Operational definition*	Sample question
TDF11: Environmental context and resources	The role of environmental factors, i.e., workload or lack of other resources in reducing the likelihood of performing hand hygiene	Do you think washing is something that everyone must follow? To prevent the spread of infection
TDF12: Social influences	The role of peers in influencing hand hygiene behaviour	The approval and support of the hospital. Makes you dare remind colleagues and doctors to wash their hands
TDF13: Emotion	Emotions that may affect hand hygiene behaviour	Hand washing is boring
TDF14: Behavioural regulation	Anything aimed at managing or changing objectively observed or measured actions, for example, self-monitoring.	Do you think nurse no need to perform hand washing after taking off gloves because it has no directly contact to patient

*Operation definitions are adapted from Cane *et al*., 2012

TDF = Theoretical Domains Framework

C.3: Participants of focus groups according their departments

Type of HCWs	Department				
	Medicine	Surgery	Pediatric	Obstetrics and Gynecology	Total
Registered nurses	3	4	2	1	10
Infection control ward nurses	3	4	2	1	10
Nurse-aids	3	4	2	1	10
Workers	1	0	1	0	2
Total	10	12	7	3	32

C.4: Descriptive data of semi-structured interview participants (n = 5)

Interview No.	Gender	Age (year)	Role type	Work area	Work status
SI1	Male	51	Head of infection control team	Physician (pediatric, infection disease)	Full-time
SI2	Female	47	Head of laboratory department	Lab technician	Full-time
SI3	Male	58	Head of surgical department	Physician (surgery)	Full-time
SI4	Male	59	Deputy director	Physician (surgery)	Full-time
SI5	Male	56	Head of eye-nose-throat department	Physician	Full-time

C.5: Summary of current knowledge of hand hygiene from participants (N = 1,582)

	Knowledge on hand hygiene					
	Mean	**Median**	**SD**	**Min**	**Max**	**N (%)**
Overall	14.3	15	2.6	0	22	1,582 (100 %)
Sex						
Male	13.8	14	3.0	0	20	272 (19.7 %)
Female	14.5	15	2.5	0	22	1,310 (80.3 %)
Year of working experience						
< 1 year	14.6	15	2.1	1	19	157 (9.3 %)
2 – 5 years	14.5	15	2.5	0	22	517 (30.5 %)
6 – 10 years	14.4	15	2.3	2	20	168 (9.9 %)
11 – 20 years	14.6	15	2.2	0	19	300 (17.7 %)
> 20 years	13.8	14	3.2	0	20	381 (29.1 %)
Type of healthcare workers						
Physicians	14.5	14	2.3	10	19	13 (7.2 %)
Nurses	14.5	15	2.3	0	22	812 (47.8 %)
Auxiliaries	13.8	14	3.3	0	18	458 (26.9 %)
Nursing students	14.7	15	1.9	1	19	299 (18.0 %)
Ward type						
ICU	14.8	15	2.2	0	21	370 (21.9 %)
Non-ICU	14.1	15	2.7	0	20	778 (46.1 %)

N = number of respondents of total study population, SD = Standard deviation, ICU = Intensive care unit

C.5: Summary of current knowledge of hand hygiene from participants (N = 1,582) (cont.)

	Knowledge on hand hygiene					
	Mean	**Median**	**SD**	**Min**	**Max**	**N (%)**
Department						
Eye Ear Nose Throat	13.9	14	1.8	7	17	55 (3.3 %)
Obstetrics and Gynecology	14.2	15	3.2	0	22	203 (12.0 %)
Medicine	14.1	15	2.8	0	19	259 (15.3 %)
Peadiatric	14.4	15	2.7	0	19	195 (11.6 %)
Surgery	14.3	15	2.6	0	21	552 (25.2 %)

N = number of respondents of total study population, SD = Standard deviation, ICU = Intensive care unit

C.6: Summary of self-reporting on hand hygiene compliance from participants (n = 1,126)

	% Hand hygiene by self-reporting					
	Mean	**Median**	**SD**	**Min**	**Max**	**N (%)**
Overall	79.2	80	18.3	0	100	1,126 (100 %)
Sex						
Male	76.0	80	23.0	0	100	181 (16.1 %)
Female	79.8	80	17.2	0	100	945 (83.9 %)
Year of working experience						
< 1 year	80.9	80	15.4	0	100	132 (11.7 %)
2 – 5 years	79.8	80	17.8	0	100	379 (33.7 %)
6 – 10 years	80.7	80	17.1	0	100	116 (10.3 %)
11 – 20 years	77.3	80	20.6	0	100	213 (18.9 %)
> 20 years	78.5	80	19.3	0	100	248 (22.0 %)
Type of healthcare workers						
Physicians	60.9	50	25.5	10	90	11 (1.1 %)
Nurses	80.6	80	17.8	0	100	589 (52.0 %)
Auxiliaries	75.0	80	22.0	0	100	269 (23.6 %)
Nursing students	81.3	80	12.8	20	100	257 (23.3 %)
Ward type						
ICU	75.0	80	24.6	0	100	259 (23.0 %)
Non-ICU	79.9	80	16.3	0	100	522 (46.4 %)

N = number of respondents of total study population, SD = Standard deviation, ICU = Intensive care unit

C.6: Summary of self-reporting on hand hygiene compliance from participants (n = 1,126) (cont.)

	% Hand hygiene by self-reporting					
	Mean	**Median**	**SD**	**Min**	**Max**	**N (%)**
Department						
Eye Ear Nose Throat	87.0	90	9.5	60	100	30 (2.7 %)
Obstetrics and Gynecology	80.7	90	21.5	0	100	132 (11.7 %)
Medicine	71.1	80	27.7	0	100	178 (15.8 %)
Peadiatric	81.4	80	14.3	40	100	120 (10.7 %)
Surgery	80.4	80	14.5	7	100	392 (24.3 %)

N = number of respondents of total study population, SD = Standard deviation, ICU = Intensive care unit

C.7: Summary on hand hygiene performed by all opportunities for requiring hand hygiene practices (n = 3,564)

	Hand hygiene practices			
	Not performed n (%)	**Performed incorrectly n (%)**	**Performed correctly n (%)**	**Total n (%)**
Sex				
Male	606 (88.1 %)	22 (3.2 %)	60 (8.7 %)	688 (100 %)
Female	2,483 (86.3 %)	135 (4.7 %)	258 (9.0 %)	2,876 (100 %)
Working years				
< 1 years	190 (83.7 %)	13 (5.7 %)	24 (10.6 %)	227 (100 %)
2 – 5 years	923 (87.9 %)	42 (4.0 %)	85 (8.1 %)	1,050 (100 %)
6 – 10 years	292 (83.9 %)	14 (4.0 %)	42 (12.1 %)	348 (100.0%)
11 – 20 years	470 (85.0 %)	33 (6.0 %)	50 (9.0 %)	553 (100 %)
> 20 years	1,022 (89.4 %)	46 (4.0 %)	75 (6.6 %)	1,143 (100 %)
Type of healthcare workers				
Physicians	288 (91.7 %)	12 (3.8 %)	14 (4.5 %)	314 (100 %)
Nurses	1,497 (83.6 %)	93 (5.2 %)	201 (11.2 %)	1,791 (100 %)
Auxiliaries	854 (88.5 %)	39 (4.0 %)	72 (7.5 %)	965 (100 %)
Visitors	184 (88.0 %)	11 (5.3 %)	14 (6.7 %)	209 (100 %)
Nursing students	166 (92.2 %)	1 (0.6 %)	13 (7.2 %)	180 (100 %)
Medical students	100 (95.2 %)	1 (1.0%)	4 (3.8 %)	105 (100 %)
Ward type				
ICU	1,305 (82.8 %)	89 (5.7 %)	182 (11.6 %)	1,576 (100 %)
Non-ICU	1,591 (89.9 %)	57 (3.2 %)	121 (6.8 %)	1,769 (100 %)

n = number of respondents of part of study population, SD = Standard deviation, ICU = Intensive-care unit

C.7: Summary on hand hygiene performed by all opportunities for requiring hand hygiene practices (n = 3,564)

	Hand hygiene practices			
	Not performed n (%)	**Performed incorrectly n (%)**	**Performed correctly n (%)**	**Total n (%)**
Department				
Obstetrics and Gynecology	279 (88.0 %)	12 (3.8 %)	26 (8.2 %)	317 (100 %)
Medicine	651 (92.1 %)	26 (3.7%)	30 (4.2 %)	707 (100 %)
Peadiatric	640 (83.1 %)	40 (5.2 %)	90 (11.7 %)	770 (100 %)
Surgery	1,326 (85.5 %)	68 (4.4 %)	157 (10.1 %)	1,551 (100 %)

n = number of respondents of part of study population, SD = Standard deviation, ICU = Intensive-care unit

C.8: Summary on hand hygiene compliance of all healthcare workers (n = 364)

	% Hand hygiene compliance					
	Mean	**Median**	**SD**	**Min**	**Max**	**N (%)**
Overall	8.9	0	19.3	0	100	364 (100 %)
Sex						* *r=0.04, p=0.40*
Male	7.6	0	17.5	0	100	106 (29.1 %)
Female	9.5	0	20.0	0	100	258 (70.9 %)
Working years						**r = -0.06, p=0.19*
< 1 years	10.5	0	18.4	0	66.7	29 (8.0 %)
2 – 5 years	9.6	0	22.4	0	100	86 (23.6 %)
6 – 10 years	13.9	0	24.8	0	100	30 (8.2 %)
11 – 20 years	7.1	0	16.1	0	100	346 (95.0 %)
> 20 years	44.6	37.6	35.8	0	100	18 (5.0 %)
Type of healthcare workers						**r =-0.02, p=0.74*
Physicians	4.6	0	12.2	0	50	71 (19.5 %)
Nurses	12.8	1.4	21.0	0	100	118 (34.4 %)
Auxiliaries	8.7	0	15.9	0	100	58 (15.9 %)
Visitors	9.4	0	25.2	0	100	54 (14.8 %)
Nursing students	7.0	0	17.1	0	66.7	34 (9.3 %)
Medical students	6.0	0	20.8	0	100	29 (8.0 %)
Ward type						*r=0.16, p< 0.01
ICU	12.2	0	22.1	0	100	161 (44.2 %)
Non-ICU	6.3	0	16.3	0	100	166 (45.6 %)

n = number of respondents of part of study population, SD = Standard deviation

*Pearson correlation (*r*) is provided with *p* values (two-tailed).

C.8: Summary on hand hygiene compliance of all healthcare workers (n = 364)

	% Hand hygiene compliance					
	Mean	**Median**	**SD**	**Min**	**Max**	**N (%)**
Department						**r=0.12, p<0.05*
Obstetrics and Gynecology	9.5	0	13.9	0	50	28 (7.7 %)
Medical	5.0	0	16.2	0	100	94 (25.8 %)
Peadiatric	9.9	0	18.1	0	100	53 (14.6 %)
Surgical	11.5	0	22.4	0	100	152 (41.8 %)
Indication						**r*=0.06, *p*=0.30
Before touching a patient	5.2	0	12.5	0	66.7	72 (19.8 %)
After touching a patient	10.9	0	20.8	0	100	86 (23.6 %)
Before clean/aseptic procedures	8.6	0	20.6	0	100	47 (12.9 %)
After body fluid exposure/risk	17.2	5.9	26.6	0	100	60 (16.5 %)
After touching patient surroundings	5.2	0	13.9	0	100	99 (27.2 %)
Number of total beds						**r*=- 0.27, *p*<0.001
8 beds	18.0	7.7	25.3	0	100	81 (22.3 %)
14 beds	5.0	0	9.1	0	28.6	19 (5.2 %)
30 beds	6.1	0	9.9	0	40	76 (20.9 %)
Bed occupancy						**r*=- 0.004, *p*=0.95
<= 100 %	5.7	0	11.4	0	50	105 (28.9 %)
> 100 %	10.3	0	21.6	0	100	259 (71.1 %)

n = number of respondents of part of study population, SD = Standard deviation

*Pearson correlation (*r*) is provided with *p* values (two-tailed).

C.9: Internal consistency of domains (α) and the distribution of response on current beliefs on hand hygiene (N = 1,582)

Theoretical domain	alpha (α)	1*	2*	3*	4*	5*	n (%)	Mean	Std. Err.	95% Confidence interval	
Knowledge	0.69	28	51	177	680	567	1,503	4.14	0.02	4.09	4.18
		1.8 %	3.2 %	11.2 %	43.0 %	35.8 %	95.0 %				
Skills	0.65	75	182	206	723	309	1,495	3.67	0.03	3.62	3.73
		4.7 %	11.5 %	13.0 %	45.7 %	19.5 %	94.5 %				
Social/professional role and	0.68	262	586	269	299	87	1,503	2.58	0.03	2.52	2.63
identity		16.7 %	37.0 %	17.0 %	18.9 %	5.5 %	95.0 %				
Beliefs about capabilities	0.65	11	8	17	406	1,062	1,504	4.66	0.02	4.63	4.69
		0.7 %	0.5 %	1.1 %	25.7 %	67.1 %	95.1 %				
Beliefs about consequences	0.64	76	3	66	412	1,025	1,582	4.46	0.02	4.41	4.51
		4.8 %	0.2 %	4.2 %	26.0 %	64.8 %	100.0%				
Intentions	0.66	0	0	3	206	1,297	1,506	4.86	0.01	4.84	4.88
		0.0 %	0.0 %	0.2 %	13.0 %	82.0 %	95.2 %				
Goals	0.65	9	6	7	327	1,154	1,503	4.74	0.01	4.71	4.76
		0.6 %	0.4 %	0.5 %	20.7 %	73.0 %	95.0 %				

*1 = strongly disagree to 5 = strongly agree

C.9: **Internal consistency of domains (α) and the distribution of response on current beliefs on hand hygiene (N = 1,582) (cont.)**

Theoretical domain	alpha (α)	1*	2*	3*	4*	5*	n (%)	Mean	Std. Err.	95% Confidence interval	
Memory, attention and	0.65	2	19	55	497	931	1,504	4.55	0.02	4.52	4.59
decision processes		0.1 %	1.2 %	3.5 %	31.4 %	58.9 %	95.1 %				
Environmental context and	0.66	10	6	8	294	1,183	1,501	4.75	0.01	4.73	4.78
resources		0.6 %	0.4 %	0.5 %	18.6 %	74.8 %	94.9 %				
Social influences	0.64	76	16	259	938	293	1,582	3.86	0.02	3.81	3.90
		4.8 %	1.0 %	16.4 %	59.3 %	18.5 %	100.0 %				
Emotion	0.64	22	65	83	643	686	1,499	4.27	0.02	4.23	4.32
		1.4 %	4.1 %	5.3 %	40.6 %	43.4 %	94.8 %				
Behavioural regulation	0.64	49	154	196	706	399	1,504	3.83	0.03	3.78	3.88
		3.1 %	9.7 %	12.4 %	44.6 %	25.2 %	95.1 %				

*1 = strongly disagree to 5 = strongly agree

C.10: Correlations between theoretical domains about hand hygiene among participants (N = 1,582)

	Knowledge	Self-reporting	TDF1	TDF2	TDF3	TDF4	TDF6	TDF8	TDF9	TDF10	TDF11	TDF12	TDF13	TDF14
Knowledge	1													
Self-reporting	0.05	1												
TDF1	0.01	- 0.05	1											
TDF2	0.02	0.10**	- 0.03	1										
TDF3	- 0.04	0.03	- 0.02	0.16***	1									
TDF4	0.07*	0.10***	0.21***	0.11***	- 0.01	1								
TDF6	0.18***	0.08**	0.06*	0.19***	0.13***	0.27***	1							
TDF8	0.10***	0.14***	0.11***	0.16***	0.05	0.33***	0.27***	1						
TDF9	0.09***	0.12***	0.15***	0.15***	0.02	0.41***	0.28***	0.42***	1					
TDF10	0.12***	0.17***	0.12***	0.19***	0.08**	0.29***	0.20***	0.42***	0.33***	1				
TDF11	0.05*	0.15***	0.15***	0.09***	- 0.05	0.44***	0.31***	0.32***	0.38***	0.26***	1			
TDF12	0.13***	0.09**	0.10***	0.23***	0.30***	0.14***	0.65***	0.17***	0.17***	0.21***	0.13***	1		
TDF13	0.02	0.09**	0.004	0.46***	0.15***	0.15***	0.30***	0.19***	0.16***	0.12***	0.15***	0.15***	1	
TDF14	- 0.04	0.07*	- 0.003	0.27***	0.23***	0.14***	0.35***	0.18***	0.19***	0.19***	0.12***	0.19***	0.31***	1

*p< .05; **p< .01; ***p< .001 (two-tailed)

NOTE: TDF1 = Knowledge; TDF2 = Skills; TDF3 = Social/professional role and identity; TDF4 = Beliefs about capabilities; TDF6 = Beliefs about consequences; TDF8 = Intentions; TDF9 = Goals; TDF10 = Memory, attention and decision processes; TDF11 = Environmental context and resources; TDF12 = Social influences; TDF13 = Emotion; TDF14 = Behavioural regulation

C.11: Correlations of performed hand hygiene practice between theoretical domains among participants (n = 364)

	% HH compliance	% performed HH	% correctly performed HH	Knowledge score	Self-reporting	TDF1	TDF2	TDF3	TDF4	TDF6	TDF8	TDF9	TDF10	TDF11	TDF12	TDF13	TDF14
% compliance	1																
% performed	0.91***	1															
% correctly performed	0.75***	0.67***	1														
Knowledge score	0.01	0.05	-0.10	1													
Self-reporting	0.04	0.07	0.03	0.07	1												
TDF1	0.05	0.09	0.07	0.01	0.05	1											
TDF2	-0.01	-0.02	-0.03	0.18*	-0.02	-0.11	1										
TDF3	-0.16*	-0.17*	-0.03	-0.08	-0.03	0.003	0.20**	1									
TDF4	0.10	0.11	0.12	0.01	0.18*	0.22**	0.07	-0.09	1								
TDF6	-0.04	-0.02	-0.01	0.10	0.05	0.06	0.25***	0.22**	0.27***	1							
TDF8	-0.02	-0.02	-0.05	0.17*	0.09	0.24***	0.07	0.02	0.29***	0.25***	1						
TDF9	0.04	0.06	-0.0007	0.08	0.16*	0.17*	0.13	0.07	0.35***	0.31***	0.52***	1					
TDF10	-0.07	-0.05	-0.15*	0.15*	0.14	0.08	0.04	0.06	0.31***	0.24***	0.28***	0.45***	1				
TDF11	0.05	0.04	0.11	0.08	0.21*	0.09	0.04	-0.03	0.62***	0.31***	0.24***	0.27***	0.27***	1			
TDF12	-0.07	-0.13	-0.02	0.02	-0.01	-0.04	0.25***	0.48***	0.14	0.15*	0.11	0.17*	0.07	0.12	1		
TDF13	0.002	-0.01	0.03	0.10	0.13	-0.19**	0.41***	0.16*	0.11	0.39***	0.17*	0.12	-0.01	0.18*	0.18**	1	
TDF14	0.06	0.02	0.02	0.09	-0.04	-0.13	0.35***	0.35***	0.03	0.51***	0.10	0.24***	0.16*	0.16*	0.24***	0.41***	1

*p< .05; **p< .01; ***p< .001 (two-tailed)

NOTE: HH = Hand hygiene; TDF1 = Knowledge; TDF2 = Skills; TDF3 = Social/professional role and identity; TDF4 = Beliefs about capabilities; TDF6 = Beliefs about consequences; TDF8 = Intentions; TDF9 = Goals; TDF10 = Memory, attention and decision processes; TDF11 = Environmental context and resources; TDF12 = Social influences; TDF13 = Emotion; TDF14 = Behavioural regulation

Appendix D

Chapter 5 Supplementary

MUTM 2012-042-01

CERTIFICATE OF ETHICAL APPROVAL
Ethics Committee of the Faculty of Tropical Medicine, Mahidol University
420/6 Ratchawithi Rd., Ratchatheewee, Bangkok 10400, Thailand

---

This Certificate of Ethical Approval (MUTM 2012-042-01) applies to the

Project entitled: A stepped wedge cluster randomised controlled trial to evaluate the impact of a multimodal hand hygiene intervention at Sappasithiprasong Hospital, Ubon Ratchathani

EC Submission No.: TMEC 12-009

with the following relevant documents:

1) Research Proposal (FTM ECF-019-02); English version 1.2 date 20 August 2012
2) Participant Information Sheet (FTM ECF-020-00); Thai version 1.1 date 20 August 2012
3) Informed Consent Form (FTM ECF-021-02); Thai version 1.1 date 20 August 2012
4) Questionnaires Form; Thai version 1.1 date 23 July 2012
5) Observation Form; Thai version 1.1 date 23 July 2012
6) Case Record Form; English version 1.0 date 9 January 2012

Principal Investigator: Dr. Direk Limmathurotsakul

Affiliation: Department of Tropical Hygiene,
Faculty of Tropical Medicine, Mahidol University

This project has been approved for the period
from 29 August 2012 to 28 August 2013

The Ethics Committee of Faculty of Tropical Medicine certify that we are in compliance with Declaration of Helsinki, ICH Guidelines for Good Clinical Practice and other International Guidelines for Human Research Protection.

Signature ....

(Prof. Srisin Khusmith)

Chairperson (Panel 2)
Ethics Committee of the
Faculty of Tropical Medicine
Date ...31 AUG 2012...

Signature ...Pornpimon Adams...

(Mrs. Pornpimon Adams)

Member and Secretary
Ethics Committee of the
Faculty of Tropical Medicine
Date ...31 AUG 2012...

คู่มือโครงการวิจัย

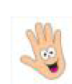
เรื่อง : ศึกษาเปรียบเทียบแบบสุ่มเป็นขั้นเพื่อประเมินผลการส่งเสริมการล้างมือในโรงพยาบาลสรรพสิทธิประสงค์ จ.อุบลราชธานี " A Stepped Wedge Cluster Randomised Controlled Trial to Evaluate the Impact of a Multimodal Hand Hygiene Intervention at Sappasitthiprasong Hospital, Ubon Ratchatani "

วัตถุประสงค์หลัก
เพื่อประเมินพฤติกรรมการล้างมือของเจ้าหน้าที่ทางการแพทย์ที่ได้รับการส่งเสริมการล้างมือตามแนวทางขององค์การอนามัยโลก (WHO) ด้วยการสังเกตการปฏิบัติตามคาแนะนาของ 5 ข้อบ่งชี้ในการทาความสะอาดมือเพื่อการพยาบาล

ระยะเวลาดาเนินโครงการ
ตั้งแต่วันที่ 1 เมษายน พ.ศ. 2556 ถึงวันที่ 31 ตุลาคม พ.ศ 2557

เจ้าหน้าที่วิจัย

1. นายแพทย์ปราโมทย์ ศรีสาอางค์	ประธานคณะกรรมการงานป้องกันและควบคุมการติดเชื้อในโรงพยาบาล
2. นางศิริรัตน์ เชาวรัตน์	หัวหน้ากลุ่มงานป้องกันและควบคุมการติดเชื้อในโรงพยาบาล
3. นางสมบูรณ์ นันตโลหิต	เจ้าหน้าที่กลุ่มงานป้องกันและควบคุมการติดเชื้อในโรงพยาบาล
4. นางสมสมัย บุญส่อง	เจ้าหน้าที่กลุ่มงานป้องกันและควบคุมการติดเชื้อในโรงพยาบาล
5. นางสาวชุติมา อ่อนสอาด	เจ้าหน้าที่กลุ่มงานป้องกันและควบคุมการติดเชื้อในโรงพยาบาล
6. นายแพทย์ดิเรก ลิ้มมธุรสกุล	ผู้วิจัยหลัก
7. นางสาวมะลิวัลย์ หงษ์สุวรรณ	พยาบาลวิชาชีพ
8. นางสาวปิยวรรณ วิลาบุตร	ผู้ช่วยเจ้าหน้าที่วิจัย
9. นางสาวเยาวลักษณ์ แหวนวงษ์	ผู้ช่วยเจ้าหน้าที่วิจัย

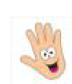


รายละเอียดการศึกษา

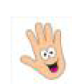
โรคหลายโรคติดต่อโดยมีมือเป็นตัวนำเชื้อโรคเข้าสู่ร่างกาย รวมไปถึงการติดเชื้อที่เกี่ยวเนื่องจากการรับการรักษาในโรงพยาบาลเป็นสาเหตุสำคัญของการเจ็บป่วยและการตายทั่วโลก และโดยเฉพาะอย่างยิ่งในโรงพยาบาลที่มีทรัพยากรจำกัดอย่างมาก การรักษาสุขลักษณะของเจ้าหน้าที่ทางการแพทย์ ซึ่งรวมถึงการล้างมือที่ดีขึ้น) โดยเฉพาะอย่างยิ่งกับการใช้งานที่เพิ่มขึ้นของแอลกอฮอล์เพื่อการล้างมือ (ในการติดต่อสัมผัสกับผู้ป่วยเป็นวิธีที่มีประสิทธิภาพมากที่สุดของการลดการติดเชื้อดังกล่าว <u>การล้างมือ (Hand Hygiene)</u> เป็นมาตรการสำคัญที่ช่วยป้องกันและลดอุบัติการณ์ของการติดเชื้อในโรงพยาบาลและเป็นมาตรการที่มีประสิทธิภาพ รวดเร็ว ประหยัดค่าใช้จ่ายที่สุด *ดังนั้นจึงจำเป็นที่เจ้าหน้าที่ทางการแพทย์ต้องล้างมืออย่างถูกวิธี*

ในการนี้ คณะผู้วิจัยโรงพยาบาลสรรพสิทธิประสงค์จังหวัดอุบลราชธานี โดย นายแพทย์ปราโมทย์ ศรีสำอางค์ และงานป้องกันและควบคุมการติดเชื้อในโรงพยาบาล ร่วมกับนายแพทย์ดิเรก ลิ้มมธุรสกุล อาจารย์ประจำหน่วยวิจัยโรคเขตร้อนมหิดล-อ๊อกซ์ฟอร์ด คณะเวชศาสตร์เขตร้อน มหาวิทยาลัยมหิดล เล็งเห็นความสำคัญของ<u>การส่งเสริมการล้างมือ (Hand Hygiene)ในหมู่เจ้าหน้าที่ของโรงพยาบาล</u> จึงได้มีการตกลงร่วมมือที่จะทำโครงการวิจัย เรื่อง "การศึกษาเปรียบเทียบแบบสุ่มเป็นขั้นเพื่อประเมินผลการส่งเสริมการล้างมือในโรงพยาบาลสรรพสิทธิประสงค์ จ. อุบลราชธานี" คณะผู้วิจัยจึงได้จัดทำคู่มือนี้ขึ้นมาเพื่อเป็นแนวทางในการส่งเสริมการล้างมือในหมู่เจ้าหน้าที่ทางการแพทย์ให้สอดคล้องกับแนวทางในการล้างมือขององค์การอนามัยโลก(WHO Guideline on Hand Hygiene in Health Care)

การศึกษานี้เป็นการศึกษาเปรียบเทียบแบบสุ่มเป็นขั้นแบบไปข้างหน้า ซึ่งจะทำการศึกษาในเจ้าหน้าที่ทางการแพทย์ในหอผู้ป่วยในทุกหอผู้ป่วยทั้งหมด 58 หอผู้ป่วย โรงพยาบาลสรรพสิทธิประสงค์) ขนาด1 , 000 เตียง (จังหวัดอุบลราชธานี รูปแบบการศึกษาแบบ stepped wedge เป็นการศึกษาประเภทหนึ่งของการสุ่มตัวอย่างเปรียบเทียบ ซึ่งการศึกษาประเภทนี้เหมาะสมที่จะทำการศึกษาเมื่อมีความเชื่อว่ากระตุ้นการล้างมืออย่างต่อเนื่องจะเป็นประโยชน์ และถ้าทำการสุ่มเลือกให้การกระตุ้นล้างมือเพียงแค่หอผู้ป่วยใดหอผู้ป่วยหนึ่งนั้น จะเป็นการไม่เหมาะสม และผิดต่อจริยธรรมทางการแพทย์ การกระตุ้นการล้างมืออย่างต่อเนื่องดังกล่าวจะถูกส่งผ่านโดยเจ้าหน้าที่วิจัยและพยาบาลผู้รับผิดชอบการติดเชื้อในแผนกผู้ป่วยในที่จะได้รับการฝึกอบรมเพิ่มเติม



ผู้วิจัยคาดหวังว่า ผลการศึกษาจะสามารถนำไปใช้ได้กับโรงพยาบาลอื่นๆ ที่มีความจำกัดทางด้านทรัพยากร ในในประเทศไทยและประเทศกำลังพัฒนาอื่นๆ นอกจากนี้ผลการวิจัยจะให้ข้อมูลที่สำคัญในการประเมินทางเศรษฐศาสตร์ของการกระตุ้นการล้างมือและผลในการควบคุมการติดเชื้อ เพื่อพิจารณาอย่างครอบคลุมว่าการกระตุ้นดังกล่าวว่ามีแนวโน้มที่จะที่มีประสิทธิภาพอย่างไร



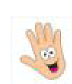
การส่งเสริมการล้างมือตามแนวทางขององค์การอนามัยโลก

โรคติดเชื้อในโรงพยาบาลเป็นโรคติดเชื้อที่รุนแรงและมีผลกระทบทางเศรษฐกิจอย่างมีนัยสำคัญทางสถิติกับผู้ป่วยและระบบดูแลสุขภาพในโลก ดังนั้นการทำความสะอาดมือที่ดี เป็นงานที่ง่ายและเป็นวิธีที่เหมาะสมที่จะสามารถช่วยชีวิตผู้ป่วยได้

องค์การอนามัยโลกได้พัฒนาหลักฐานเกี่ยวกับคู่มือการทำความสะอาดมือในสถานบริการเพื่อสนับสนุนสถานบริการสุขภาพเพื่อให้มีการพัฒนาการทำความสะอาดมือและการลดลงของโรคติดเชื้อในโรงพยาบาล

คู่มือการดำเนินการนี้ได้รับการพัฒนาขึ้นเพื่อช่วยสถานบริการสุขภาพในการดำเนินการพัฒนาการทำความสะอาดมือตามคู่มือเกี่ยวกับการทำความสะอาดมือในสถานบริการขององค์การอนามัยโลก

กลยุทธ์ที่ได้รับการอธิบายในคู่มือการดำเนินการนี้ได้รับการออกแบบเพื่อใช้กับสถานบริการสุขภาพอื่นๆ โดยไม่คำนึงถึงระดับของทรัพยากรหรือสถานบริการได้เริ่มต้นดำเนินการเกี่ยวกับการทำความสะอาดมือไปแล้วหรือไม่ วิธีการนี้มุ่งเน้นไปที่การพัฒนาการทำความสะอาดมือโดยบุคลากรสุขภาพที่ดำเนินงานกับผู้ป่วยผ่านการดำเนินงานที่นำเสนอโดยกลยุทธ์ การพัฒนาโครงสร้างการในทำความสะอาดมือพร้อมด้วยการเพิ่มความรู้และการรับรู้เกี่ยวกับการทำความสะอาดมือและโรคติดเชื้อในโรงพยาบาล และสภาพแวดล้อมที่ปลอดภัยสำหรับผู้ป่วยจะหมายถึงการดำเนินงานที่ประสบผลสำเร็จ เป้าหมายสูงสุดคือการลดทั้งการแพร่กระจายของการติดเชื้อและการดื้อต่อเชื้อโรคหลายชนิดตลอดจนจำนวนของผู้ป่วยที่สามารถป้องกันโรคติดเชื้อในโรงพยาบาลและป้องกันการสูญเสียทรัพยากรและรักษาชีวิต



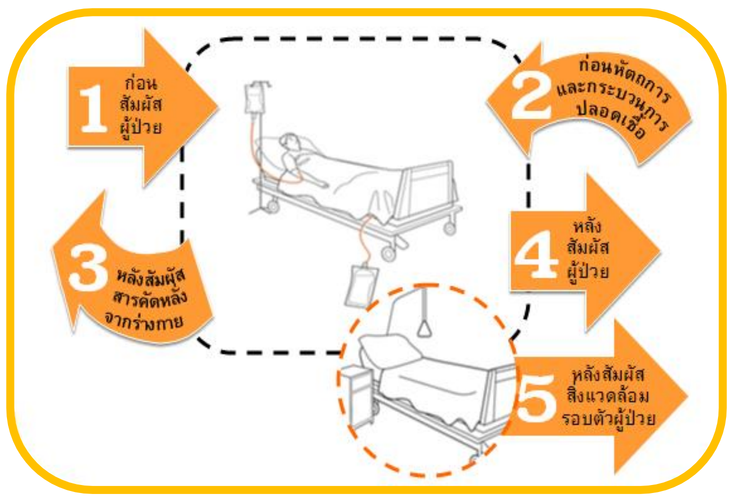
กลยุทธ์ในการพัฒนาการทำความสะอาดมือขององค์การอนามัย

1. **<u>การเปลี่ยนแปลงระบบ(System change):</u>** ทำให้มั่นใจได้ว่าโครงสร้างพื้นฐานที่จำเป็นอยู่ในที่ที่บุคลากรสามารถเข้าถึงได้ เพื่อปฏิบัติในการทำความสะอาดมือ ซึ่งประกอบด้วยสององค์ประกอบที่จำเป็นดังนี้

- สามารถเข้าถึงความปลอดภัย ระบบจ่ายน้ำที่ต่อเนื่องรวมถึงสบู่และผ้าเช็ดมือ
- เข้าถึงแอลกอฮอล์ถูมือ ณ จุดดูแลผู้ป่วยได้อย่างง่ายดาย

2. **<u>การอบรมให้ความรู้/(Training and education):</u>** จัดให้มีการสอนเป็นประจำเกี่ยวกับความสำคัญในการทำความสะอาดมือ บนพื้นฐานของ " 5 ข้อบ่งชี้ในการทำความสะอาดมือเพื่อการพยาบาลและกระบวนการที่ " ถูกต้องสำหรับการถูมือและการล้างมือให้แก่บุคลากรสุขภาพทุกคน

<u>5 ข้อบ่งชี้ในการทำความสะอาดมือเพื่อการพยาบาล</u>



6

3. **<u>การประเมินและให้ข้อมูลย้อนกลับ(Evaluation and feedback):</u>** ตรวจสอบการปฏิบัติและโครงสร้างพื้นฐานในการทำความสะอาดมือ พร้อมด้วยการรับรู้และความรู้ที่เกี่ยวข้องในบุคลากรสุขภาพ ขณะที่ให้ข้อมูลเกี่ยวกับประสิทธิภาพในการปฏิบัติ และให้ข้อมูลย้อนกลับไปยังบุคลากร

4. **<u>สิ่งเตือนใจในสถานบริการ(Reminder at workplace):</u>** กระตุ้นเตือนบุคลากรสุขภาพเกี่ยวกับความสำคัญเกี่ยวกับการทำความสะอาดมือและเกี่ยวกับตัวชี้วัดที่เหมาะสมรวมถึงกระบวนการในการดำเนินการ

8

5. **<u>การสร้างสภาพแวดล้อมที่ส่งเสริมการล้างมือในหอผู้ป่วย(Ward safety climate):</u>** สร้างสภาพแวดล้อมและการรับรู้ซึ่งส่งเสริมให้มีความตระหนักที่เพิ่มขึ้นเกี่ยวกับประเด็นความปลอดภัยของผู้ป่วย ในขณะที่มีการรับประกันว่าการพิจารณาเกี่ยวกับการพัฒนาการทำความสะอาดมือเป็นลำดับความสำคัญขั้นสูงในทุกระดับ ซึ่งประกอบด้วย

- การเข้ามามีส่วนร่วมในกิจกรรรมทั้งในระดับแผนก ระดับหอผู้ป่วยและระดับบุคคล
- การตระหนักถึงความสามารถส่วนบุคคลและสถาบันในการเปลี่ยนแปลงและพัฒนาประสิทธิภาพ) และ(ส่วนบุคคล
- การมีส่วนร่วมกับผู้ป่วยและองค์กรผู้ป่วย

ขั้นตอนดำเนินการ

ประกอบด้วย 5 ขั้นตอนในการดำเนินการตามลำดับ ดังนี้

ขั้นตอนที่ 1: การประเมินพื้นฐาน สร้างองค์ความรู้เกี่ยวกับสถานการณ์ปัจจุบัน –ของหอผู้ป่วยของท่าน

- ดำเนินการประเมินพื้นฐานเกี่ยวกับการปฏิบัติ ,การรับรู้ ,ความรู้และโครงสร้างที่สามารถใช้ได้ในการทำความสะอาดมือ

**ซึ่งในการศึกษานี้ท่านจะต้องเลือกกลยุทธ์การส่งเสริมการล้างมือที่คิดว่าเหมาะสมกับหอผู้ป่วยของท่าน หลังจากนั้นนำไปสู่แนวทางการปฏิบัติ ซึ่งในแต่ละกลยุทธ์จะมีแนวทางการประเมินที่แตกต่างกัน ดังต่อไปนี้

1) การเปลี่ยนแปลงระบบ(System change)

   <u>ประเมินองค์ประกอบที่จำเป็นต่อการล้างมือทุกเดือน</u>

2) การอบรมให้คว/ามรู้(Training and education)

   <u>ประเมินความรู้พื้นฐานของการล้างมือและการติดเชื้อในโรงพยาบาล ของเจ้าหน้าที่ในหอผู้ป่วยทุกคนในหอผู้ป่วย ทุก 3 เดือน เพื่อหาจัดกลุ่มการอบรมให้เหมาะสมกับบุคคลโดยคณะวิจัยจะเป็นผู้เตรียมแบบสอบถามพร้อมทั้งเอกสารประกอบการสอนให้แก่หอผู้ป่วย</u>

3) การประเมินและให้ข้อมูลย้อนกลับ(Evaluation and feedback)

   <u>ประเมินสถานการณ์การล้างมือและอัตรการติดเชื้อในโรงพยาบาลในหอผู้ป่วยของท่าน</u>

   <u>ค้นหาผู้ที่ปฏิบัติการล้างมืออย่างถูกต้อง และแต่งตั้งให้เป็น "Hand hygiene star" เพื่อเป็นผู้ช่วยในการให้ข้อมูลย้อนกลับกับเจ้าหน้าที่ในหอผู้ป่วยที่ล้างมือไม่ถูกต้อง โดยจะต้องมีการคัดเลือก</u>

4) สิ่งเตือนใจในสถานบริการ(Reminder at workplace)

   <u>ประเมินว่าต้องการสิ่งเตือนใจประเภทใดบ้างและจำนวนเท่าไหร่โดยคณะวิจัยจะเป็นผู้เตรียมแบบสิ่งเตือนใจให้แก่หอผู้ป่วย</u>

5) การสร้างสภาพแวดล้อมที่ส่งเสริมการล้างมือในหอผู้ป่วย(Ward safety climate)

6) แนวทางที่ออผู้ป่วยริเริ่มขึ้นเอง

ขั้นตอนที่ 2: การเตรียมสถานบริการสำหรับดำเนินการ

- สร้างความมั่นใจว่ามีการเตรียมความพร้อมของสถาบัน รวมถึงการได้มาซึ่งทรัพยากรที่จำเป็นทั้ง) ,(ทรัพยากรบุคคลและการเงินการวางโครงสร้าง ,ระบุผู้นำที่สำคัญเพื่อเป็นหลักในโปรแกรมรวมถึงผู้ประสานงานและรองผู้ประสานงาน โดยแผนที่เหมาะสมจะต้องประกอบด้วยแผนที่ทางเดินยุทธศาสตร์ที่ชัดเจนสำหรับโปรแกรมทั้งหมด

ขั้นตอนที่ 3: ดำเนินการพัฒนากิจกรรม

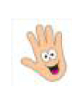
- ดำเนินการประเมินพื้นฐานเกี่ยวกับการปฏิบัติ ,การรับรู้ ,ความรู้และโครงสร้างที่สามารถใช้ได้ในการทำความสะอาดมือ

ขั้นตอนที่ 4: ติดตามประเมินผล ประเมินผลกระทบจากการดำเนินงาน –
ดำเนินการประเมินพื้นฐานเกี่ยวกับการปฏิบัติความรู้และโครงสร้างที่สามารถใช้ได้ในการทำความ ,การรับรู้ , สะอาดมือ

ขั้นตอนที่ 5: วางแผนอย่างต่อเนื่องและทบทวน

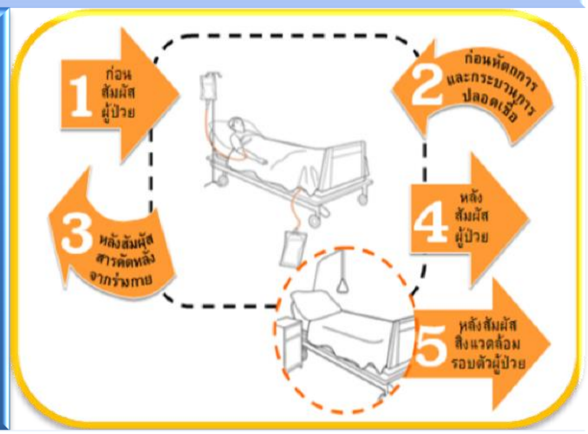
- พัฒนาแผนปฏิบัติและทบทวนวงจรอย่างต่อเนื่อง เพื่อให้มั่นใจถึงความยั่งยืนในระยะยาว

วัตถุประสงค์ทั้งหมดนี้เพื่อปลูกฝังการทำความสะอาดมือให้เป็นส่วนหนึ่งที่สำคัญของวัฒนธรรมในสถานบริการสุขภาพ



การพัฒนาการทำความสะอาดมือตามแนวทางขององค์การอนามัยโลก

5 กลยุทธ์ของ องค์การอนามัยโลก



ขั้นตอนดำเนินการ

1. การประเมินพื้นฐาน
2. การเตรียมสถานบริการ
3. การดำเนินการ
4. การติดตามประเมินผล
5. ทบทวนและวางแผน

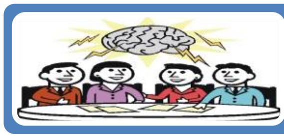
ทางคณะผู้วิจัยได้มีการประยุกต์นำแนวทางการส่งเสริมการล้างมือตาม 5 กลยุทธ์ขององค์การอนามัยโลก และเปิดโอกาสให้ทางหอผู้ป่วยพัฒนากลยุทธ์ของตนเองได้หากในแต่ละหอผู้ป่วยคิดเห็นว่าต้องการส่งเสริมการล้างมือในแนวทางที่แตกต่างจาก แนวทางขององค์การอนามัยโลก ซึ่งกลยุทธ์ของการศึกษานี้จะมีทั้งทั้งหมด 6 แนวทาง ดังนี้

การเปลี่ยนแปลงระบบ (System change)

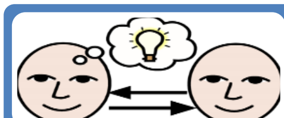
การอบรม/ให้ความรู้ (Training and education)

การประเมินและให้ข้อมูลย้อนกลับ (Evaluation and feedback)

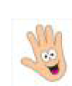
สิ่งเตือนใจในสถานบริการ (Reminder at workplace)



การสร้างสภาพแวดล้อมที่ส่งเสริมการล้างมือในหอผู้ป่วย (Ward safety climate)



แนวทางที่หอผู้ป่วยริเริ่มขึ้นเอง (Creative idea)



ล้างมือให้สะอาด...ปราศจากโรค

เอกสารชี้แจงโครงการวิจัย

เรื่อง : ศึกษาเปรียบเทียบแบบสุ่มเป็นขั้นเพื่อประเมินผลการส่งเสริมการล้างมือในโรงพยาบาลสรรพสิทธิประสงค์ จ.อุบลราชธานี " A Stepped Wedge Cluster Randomised Controlled Trial to Evaluate the Impact of a Multimodal Hand Hygiene Intervention at Sappasitthiprasong Hospital, Ubon Ratchatani "

<u>วัตถุประสงค์หลัก</u>

เพื่อประเมินพฤติกรรมการล้างมือของเจ้าหน้าที่ทางการแพทย์ที่ได้รับการส่งเสริมการล้างมือตามแนวทางขององค์การอนามัยโลก (WHO) ด้วยการสังเกตการปฏิบัติตามคำแนะนำของ 5 ข้อบ่งชี้ในการทำความสะอาดมือเพื่อการพยาบาล

<u>ระยะเวลาดำเนินโครงการ</u>

ตั้งแต่วันที่ 1 เมษายน พ.ศ. 2556 ถึงวันที่ 31 ตุลาคม พ.ศ 2557

<u>เจ้าหน้าที่วิจัย</u>

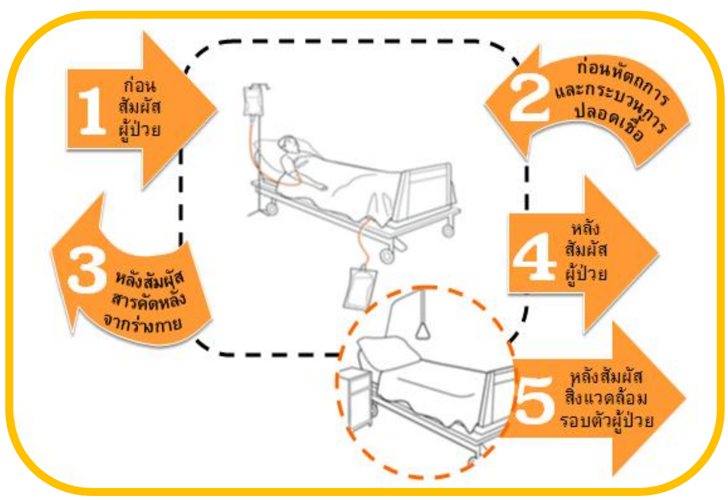
1. นายแพทย์ปราโมทย์ ศรีสำอางค์	ประธานคณะกรรมการงานป้องกันและควบคุมการติดเชื้อในโรงพยาบาล
2. นางศิริรัตน์ เชาวรัตน์	หัวหน้ากลุ่มงานป้องกันและควบคุมการติดเชื้อในโรงพยาบาล
3. นางสมบูรณ์ นันตโลหิต	เจ้าหน้าที่กลุ่มงานป้องกันและควบคุมการติดเชื้อในโรงพยาบาล
4. นางสมสมัย บุญส่อง	เจ้าหน้าที่กลุ่มงานป้องกันและควบคุมการติดเชื้อในโรงพยาบาล
5. นางสาวชุติมา อ่อนสอาด	เจ้าหน้าที่กลุ่มงานป้องกันและควบคุมการติดเชื้อในโรงพยาบาล
6. นายแพทย์ดิเรก ลิ้มมธุรสกุล	ผู้วิจัยหลัก
7. นางสาวมะลิวัลย์ หงษ์สุวรรณ	พยาบาลวิชาชีพ
8. นางสาวปิยวรรณ วิลาบุตร	ผู้ช่วยเจ้าหน้าที่วิจัย
9. นางสาวเยาวลักษณ์ แหวนวงษ์	ผู้ช่วยเจ้าหน้าที่วิจัย

รายละเอียดของกลยุทธ์ในการส่งเสริมการทำความสะอาดมือ

กลยุทธ์ในการพัฒนาการทำความสะอาดมือขององค์การอนามัยโลกที่จะนำมาประยุกต์ใช้ให้สอดคล้องกับแต่ละหอผู้ป่วย ได้แก่

1. **การเปลี่ยนแปลงระบบ (System change):** ทำให้มั่นใจได้ว่าโครงสร้างพื้นฐานที่จำเป็นอยู่ในที่ที่บุคลากรสามารถเข้าถึงได้ เพื่อปฏิบัติในการทำความสะอาดมือ ซึ่งประกอบด้วย 2 องค์ประกอบที่จำเป็น ดังนี้
   - สามารถเข้าถึงความปลอดภัย ระบบจ่ายน้ำที่ต่อเนื่องรวมถึงสบู่และผ้าเช็ดมือ
   - เข้าถึงแอลกอฮอล์ถูมือ ณ จุดดูแลผู้ป่วยได้อย่างง่ายดาย
2. **การอบรมให้ความรู้(Training and education):** จัดให้มีการสอนเป็นประจำเกี่ยวกับความสำคัญในการทำความสะอาดมือ บนพื้นฐานของ " 5 ข้อบ่งชี้ในการทำความสะอาดมือเพื่อการพยาบาล" และกระบวนการที่ถูกต้องสำหรับการถูมือและการล้างมือให้แก่บุคลากรสุขภาพทุกคน

   <u>5 ข้อบ่งชี้ในการทำความสะอาดมือเพื่อการพยาบาล</u>



3. **การประเมินและให้ข้อมูลย้อนกลับ (Evaluation and feedback):** ตรวจสอบการปฏิบัติและโครงสร้างพื้นฐานในการทำความสะอาดมือ พร้อมด้วยการรับรู้และความรู้ที่เกี่ยวข้องในบุคลากรสุขภาพ ขณะที่ให้ข้อมูลเกี่ยวกับประสิทธิภาพในการปฏิบัติ และให้ข้อมูลย้อนกลับไปยังบุคลากร

4. **สิ่งเตือนใจในสถานบริการ (Reminder at workplace):** กระตุ้นเตือนบุคลากรสุขภาพเกี่ยวกับความสำคัญในการทำความสะอาดมือและตัวชี้วัดที่เหมาะสม รวมถึงกระบวนการในการดำเนินการ
5. **การสร้างสภาพแวดล้อมที่ส่งเสริมการล้างมือในหอผู้ป่วย(Ward safety climate):** สร้างสภาพแวดล้อมและการรับรู้ ซึ่งส่งเสริมให้มีความตระหนักที่เพิ่มขึ้นเกี่ยวกับประเด็นความปลอดภัยของผู้ป่วย ในขณะที่มีการรับประกันว่าการพิจารณาเกี่ยวกับการพัฒนาการทำความสะอาดมือเป็นลำดับความสำคัญขั้นสูงในทุกระดับของสถานบริการ ซึ่งประกอบด้วย
    - การเข้ามามีส่วนร่วมในกิจกรรรมทั้งในระดับแผนก ระดับหอผู้ป่วยและระดับบุคคล
    - การตระหนักถึงความสามารถส่วนบุคคลและสถาบันในการเปลี่ยนแปลงและพัฒนาประสิทธิภาพส่วนบุคคล
    - การมีส่วนร่วมกับผู้ป่วยและองค์กรผู้ป่วย

<u>ทางคณะผู้วิจัย</u>ได้มีการประยุกต์นำแนวทางการส่งเสริมการล้างมือตาม 5 กลยุทธ์ขององค์การอนามัยโลก และเปิดโอกาสให้ทางหอผู้ป่วยพัฒนากลยุทธ์ของตนเองได้ หากในแต่ละหอผู้ป่วยคิดเห็นว่าต้องการส่งเสริมการล้างมือในแนวทางที่แตกต่างจากแนวทางขององค์การอนามัยโลก ซึ่งกลยุทธ์ของการศึกษาครั้งนี้จะมีทั้งหมด 6 แนวทาง ดังนี้

1. การเปลี่ยนแปลงระบบ (System change)
2. การอบรมให้ความรู้ (Training and education)
3. การประเมินและให้ข้อมูลย้อนกลับ (Evaluation and feedback)
4. สิ่งเตือนใจในสถานบริการ (Reminder at workplace)
5. การสร้างสภาพแวดล้อมที่ส่งเสริมการล้างมือในหอผู้ป่วย (Ward safety climate)
6. แนวทางที่หอผู้ป่วยริเริ่มขึ้นเอง

รายละเอียดเพิ่มเติมในแต่ละกลยุทธ์จะชี้แจงแก่แต่ละหอผู้ป่วยใน โดยคณะผู้วิจัยในวันและเวลาที่จะดำเนินการให้สิ่งกระตุ้นในการส่งเสริมการล้างมือในแต่ละหอผู้ป่วยตามที่ได้กำหนดไว้ในโครงการวิจัย

โดยคณะผู้วิจัยจะขออนุญาตดำเนินการดังนี้

1. ขออนุญาตเข้าพบหัวหน้าหอผู้ป่วยและพยาบาลควบคุมการติดเชื้อประจำหอผู้ป่วย ตามวันและเวลาที่กำหนดไว้ในโครงการวิจัย ซึ่งจะใช้เวลา 2 วัน วันละ 1 ชั่วโมงในแต่ละหอผู้ป่วย ในการดำเนินการเพื่อพัฒนาแนวทางการส่งเสริมการล้างมือให้สอดคล้องกับแนวทางขององค์การอนามัยโลก(WHO Guideline on Hand Hygiene in Health Care) และให้แต่ละหอผู้ป่วยดำเนินการตามแนวทางที่ได้ตกลงกันจนสิ้นสุดโครงการ
2. ขออนุญาตสัมภาษณ์หัวหน้าหอผู้ป่วยและพยาบาลควบคุมการติดเชื้อประจำหอผู้ป่วย ในประเด็นที่เกี่ยวข้องกับ "อุปกรณ์และค่าใช้จ่ายในการส่งเสริมการล้างมือ" ตามระยะเวลาที่กำหนดไว้ในโครงการวิจัย
3. ขอความร่วมมือเจ้าหน้าที่ประจำหอผู้ป่วยในทุกท่าน ตอบแบบสอบถามเกี่ยวกับ "ความรู้และทัศนคติที่มีต่อการล้างมือ" ทุกๆ 3 เดือนตลอดระยะเวลาดำเนินโครงการวิจัย
4. ขอความร่วมมือแต่ละหอผู้ป่วยตอบแบบสอบถามเพื่อใช้เป็นข้อมูลเบื้องต้นในการพัฒนาแนวทางการส่งเสริมการล้างมือให้สอดคล้องกับแนวทางขององค์การอนามัยโลก (WHO Guideline on Hand Hygiene in Health Care)

หลังจากที่ท่านได้ทบทวนกลยุทธ์ในการพัฒนาการทำความสะอาดมือข้างต้นแล้ว <u>ท่านคิดว่า กลยุทธ์ใดที่เหมาะสมที่จะใช้เป็นแนวทางในการส่งเสริมการล้างมือในหอผู้ป่วยของท่าน</u>

1. การเปลี่ยนแปลงระบบ (System change)

เหมาะสม เพราะ……………………………………………………………………………………………...
………
………
………
………
………
ไม่เหมาะสม เพราะ…………………………………………………………………………………………….
………
………
………
………
………

2. การอบรมให้ความรู้ (Training and education)

เหมาะสม เพราะ……………………………………………………………………………………………...

……….

……….

……….

………

………

ไม่เหมาะสม เพราะ…………………………………………………………………………………………..

………

………

………

………

……

3. การประเมินและให้ข้อมูลย้อนกลับ (Evaluation and feedback)

เหมาะสม เพราะ……………………………………………………………………………………………

……….

………

………

………

………

ไม่เหมาะสม เพราะ…………………………………………………………………………………………..

…….....

……….

……….

……….

………

4. สิ่งเตือนใจในสถานบริการ (Reminder at workplace)

เหมาะสม เพราะ………………………………………………………………………………………….

………………………………………………………………………………………………

………………………………………………………………………………………………

………………………………………………………………………………………………

………………………………………………………………………………………………

……………………………………………………………………………………………...

ไม่เหมาะสม เพราะ……………………………………………………………………………...

……………………………………………………………………………………………...

………………………………………………………………………………………………

………………………………………………………………………………………………

………………………………………………………………………………………………

………………………………………………………………………………………………

5. การสร้างสภาพแวดล้อมที่ส่งเสริมการล้างมือในหอผู้ป่วย (Ward safety climate)

เหมาะสม เพราะ………………………………………………………………………………………….

………………………………………………………………………………………………

………………………………………………………………………………………………

………………………………………………………………………………………………

………………………………………………………………………………………………

………………………………………………………………………………………………

ไม่เหมาะสม เพราะ…………………………………………………………………………….

………………………………………………………………………………………………

………………………………………………………………………………………………

………………………………………………………………………………………………

………………………………………………………………………………………………

6. **แนวทางที่หอผู้ป่วยริเริ่มขึ้นเอง** หากท่านคิดเห็นว่าต้องการส่งเสริมการล้างมือในแนวทางที่แตกต่างจากแนวทางขององค์การอนามัยโลก *โปรดแสดงความคิดเห็น*

……..

……..

……..

…….

……..

……..

……..

……………………………………………………………………………………………………….

……..

……..

……..

…….

……..

……..

……..

……………………………………………………………………………………………………….

……..

……..

……..

…….

……..

……..

……..

D.3: Description of assessment of inter-rater reliability

No.	Total opportunities	Date	Number of observers	Kappa			
				Indication	Hand hygiene practice	Step	Overall
1	118	13-Nov-13	2	0.923	0.538	0.599	0.600
2	105	14-Nov-13	2	0.975	1.000	0.946	0.884
3	105	3-Jan-14	2	0.987	0.793	0.791	0.795
4	118	31-Jan-14	2	1.000	0.968	0.935	0.919
5	118	24-Feb-14	2	0.950	0.930	0.859	1.000
6	118	21-Apr-14	3	0.840	0.950	1.000	1.000
7	118	30-May-14	3	0.974	0.932	0.832	1.000
8	120	30-Jun-14	3	1.000	0.936	0.935	1.000
9	120	1-Aug-14	3	1.000	1.000	1.000	1.000
10	120	29-Aug-14	3	0.984	0.968	0.967	0.967
11	125	26-Sep-14	3	1.000	0.779	0.777	1.000
12	110	30-Oct-14	2	1.000	1.000	1.000	1.000
13	108	27-Nov-14	2	1.000	1.000	1.000	1.000
14	116	22-Dec-14	2	1.000	1.000	1.000	1.000

D.3: Description of assessment of inter-rater reliability (cont.)

No.	Total opportunities	Date	Number of observers	Kappa			
				Indication	Hand hygiene practice	Step	Overall
15	107	30-Jan-15	2	1.000	1.000	1.000	1.000
16	113	27-Feb-15	2	1.000	1.000	1.000	1.000
17	103	30-Mar-15	2	1.000	1.000	1.000	1.000
18	106	29-Apr-15	2	1.000	1.000	1.000	1.000

D.4: Descriptive statistics for characteristics and covariates in the study by hand hygiene events vs. all observed events [*n*]

Variables	Before intervention	After intervention	Overall
Overall	8,013 vs. 12,598	4,943 vs. 8,111	12,956 vs.20,709
Sex			
Male	1,917 vs. 3,455	886 vs. 1,766	2,803 vs. 5,221
Female	6,096 vs. 9,143	4,057 vs. 6,345	10,153 vs. 15,488
Type of HCWs			
Doctor	497 vs. 500	140 vs. 140	637 vs. 640
Registered Nurse	4,244 vs. 5,705	2,702 vs. 3,746	6,946 vs. 9,451
Technical Nurse	147 vs. 202	139 vs. 231	286 vs. 433
Nursing Assistant	335 vs. 619	230 vs. 402	565 vs. 1,021
Nursing Aide	1,387 vs. 3,229	904 vs. 1,964	2,291 vs. 5,193
Worker	523 vs. 1,460	461 vs. 1,261	984 vs. 2,721
Medical Student	118 vs. 118	29 vs. 29	147 vs. 147
Nursing Student	393 vs. 393	251 vs. 251	643 vs. 644
Visitor	370 vs. 372	87 vs. 87	457 vs. 459
Ward type			
Non-ICU wards	5,032 vs. 7,797	3,468 vs. 5,636	8,500 vs. 13,433
ICU wards	2,981 vs. 4,801	1,475 vs. 2,475	4,456 vs. 7,276
Department			
Obstetrics and gynecology	176 vs. 295	652 vs. 1,162	828 vs. 1,457
Eye	35 vs. 60	163 vs. 307	198 vs. 367
Ear Nose Throat	65 vs. 108	136 vs. 256	201 vs. 364
Pediatrics	873 vs. 1,416	1,134 vs. 1,893	2,007 vs. 3,309
Medicine	2,478 vs. 3,634	1,508 vs. 2,266	3,986 vs. 5,900
Surgery	4,386 vs. 7,085	1,350 vs. 2,227	5,736 vs. 9,312

D.5: Descriptive statistics by observed opportunities [*n*] for characteristics and covariates in the study

Variable	Before intervention		After intervention		Overall	
	***n* = 34,430**	**%**	***n* = 22,646**	**%**	***n* = 57,076**	**%**
Sex						
Male	7,837	22.76	3,874	17.11	11,711	20.52
Female	26,593	77.24	18,772	82.89	45,365	79.48
Type of HCW						
Doctor	1,829	5.31	609	2.69	2,438	4.27
Registered Nurse	18,702	54.32	12,667	55.93	31,369	54.96
Technical Nurse	588	1.71	506	2.23	1,094	1.92
Nursing Assistant	1,659	4.82	1,233	5.44	2,892	5.07
Nursing Aide	6,557	19.04	4,306	19.01	10,863	19.03
Worker	2,095	6.08	1,816	8.02	3,911	6.85
Medical Student	418	1.21	101	0.45	519	0.91
Nursing Student	1,361	3.95	1,084	4.79	2,445	4.28
Visitor	1,221	3.55	324	1.43	1,545	2.71
Ward type						
Non-ICU wards	22,336	64.87	16,089	71.05	38,425	67.32
ICU wards	12,094	35.13	6,557	28.95	18,651	32.68

D.5: Descriptive statistics by observed opportunities [*n*] for characteristics and covariates in the study (cont.)

Variable	Before intervention		After intervention		Overall	
	n **= 34,430**	**%**	***n*** **= 22,646**	**%**	***n*** **= 57,076**	**%**
Department						
Obstetrics and gynecology	683	1.98	2,760	12.19	3,443	6.03
Eye	175	0.51	786	3.47	961	1.68
Ear Nose Throat	243	0.71	585	2.58	828	1.45
Paediatrics	3,418	9.93	4,804	21.21	8,222	14.41
Medicine	11,071	32.16	7,449	32.89	18,520	32.45
Surgery	18,840	54.72	6,262	27.65	25,102	43.98
Indication for performing hand hygiene						
Before touching a patient	7,904	22.96	4,802	21.2	12,706	22.26
After touching a patient	7,781	22.6	4,697	20.74	12,478	21.86
Before clean/aseptic procedures	4,266	12.39	2,604	11.5	6,870	12.04
After body fluid exposure/risk	4,780	13.88	2,668	11.78	7,448	13.05
After touching patient surroundings	9,699	28.17	7,875	34.77	17,574	30.79

D.6: Summary of characteristics of all study wards

Ward	Department*	ICU	No. of Permanent staff	No. of Visitors	Before intervention			After intervention			Overall		
					No. of Observed sessions	No.of HCW observed	No.of opportunities	No. of Observed sessions	No.of HCW observed	No.of opportunities	No. of Observed sessions	No.of HCW observed	No.of opportunities
1	Obst	no	22	38	18	108	269	56	252	665	74	360	934
2	Obst	no	24	45	5	42	68	69	325	806	74	367	874
3	Obst	no	20	18	5	31	63	67	339	741	72	370	804
4	Obst	no	21	28	20	114	283	54	246	548	74	360	831
5	Obst	no	22	33	62	310	1,000	12	41	117	74	351	1,117
6	Obst	no	26	33	8	43	149	66	302	937	74	345	1,086
7	Obst	no	26	36	16	92	220	58	259	665	74	351	885
8	Obst	no	23	63	13	87	184	60	306	671	73	393	855
9	Obst	no	22	29	10	58	139	64	293	778	74	351	917
10	Eye	no	25	20	11	60	175	63	307	786	74	367	961

*Note: Obst= Obstetrics and gynecology; ENT= Ear Nose Throat; Paed= Paediatrics; Med=Medicine; Surg= Surgery

D.6: Summary of characteristics of all study wards (cont.)

Ward	Department*	ICU	No. of Permanent staff	No. of Visitors	Before intervention			After intervention			Overall		
					No. of Observed sessions	No.of HCW observed	No.of opportunities	No. of Observed sessions	No.of HCW observed	No.of opportunities	No. of Observed sessions	No.of HCW observed	No.of opportunities
11	ENT	no	25	25	20	108	243	54	256	585	74	364	828
12	Paed	yes	26	18	65	353	707	8	42	61	73	395	768
13	Paed	yes	26	12	20	108	189	54	267	512	74	375	701
14	Paed	yes	27	33	7	47	95	67	335	964	74	382	1,059
15	Paed	yes	31	31	64	318	735	10	48	99	74	366	834
16	Med	no	33	50	50	295	1,115	24	121	595	74	416	1,710
17	Med	no	37	55	23	149	570	51	217	880	74	366	1,450
18	Med	no	32	47	64	341	1,276	9	33	86	73	374	1,362
19	Med	no	35	47	33	199	825	41	167	838	74	366	1,663
20	Med	no	36	64	65	348	1,382	9	37	165	74	385	1,547

*Note: Obst= Obstetrics and gynecology; ENT= Ear Nose Throat; Paed= Paediatrics; Med=Medicine; Surg= Surgery

D.6: Summary of characteristics of all study wards (cont.)

Ward	Department*	ICU	No. of Permanent staff	No. of Visitors	Before intervention			After intervention			Overall		
					No. of Observed sessions	No.of HCW observed	No.of opportunities	No. of Observed sessions	No.of HCW observed	No.of opportunities	No. of Observed sessions	No.of HCW observed	No.of opportunities
21	Med	no	42	43	44	251	967	30	138	558	74	389	1,525
22	Med	no	27	23	20	119	257	54	228	614	74	347	871
23	Med	yes	28	43	33	208	531	41	184	437	74	392	968
24	Med	yes	31	39	24	162	420	50	204	660	74	366	1,080
25	Med	yes	30	36	23	146	427	51	226	671	74	372	1,098
26	Med	yes	30	37	23	148	354	51	225	646	74	373	1,000
27	Med	yes	33	31	65	330	841	9	32	80	74	362	921
28	Med	no	36	13	23	139	303	51	212	559	74	351	862
29	Med	no	24	17	65	318	790	7	24	67	72	342	857
30	Med	yes	27	17	31	178	350	43	183	515	74	361	865
Total			1,530	1,742	2,367	12,598	34,430	1,839	8,111	22,646	4,206	20,709	57,076

*Note: Obst= Obstetrics and gynecology; ENT= Ear Nose Throat; Paed= Paediatrics; Med=Medicine; Surg= Surgery

D.6: Summary of characteristics of all study wards (cont.)

Ward	Department*	ICU	No. of Permanent staff	No. of Visitors	Before intervention			After intervention			Overall		
					No. of Observed sessions	No.of HCW observed	No.of opportunities	No. of Observed sessions	No.of HCW observed	No.of opportunities	No. of Observed sessions	No.of HCW observed	No.of opportunities
31	Med	yes	29	12	64	303	663	9	35	78	73	338	741
32	Surg	no	25	35	45	253	679	29	118	398	74	371	1,077
33	Surg	no	25	43	37	217	684	37	157	440	74	374	1,124
34	Surg	no	17	29	65	324	887	8	33	82	73	357	969
35	Surg	no	19	33	44	229	569	30	124	363	74	353	932
36	Surg	no	20	32	37	201	519	37	151	462	74	352	981
37	Surg	no	21	45	33	206	487	41	171	496	74	377	983
38	Surg	no	23	20	62	314	634	12	47	125	74	361	759
39	Surg	no	24	27	64	308	927	10	35	131	74	343	1,058
40	Surg	no	23	20	65	334	763	9	32	91	74	366	854

*Note: Obst= Obstetrics and gynecology; ENT= Ear Nose Throat; Paed= Paediatrics; Med=Medicine; Surg= Surgery

D.6: Summary of characteristics of all study wards (cont.)

Ward	Department*	ICU	No. of Permanent staff	No. of Visitors	Before intervention: No. of Observed sessions	Before intervention: No.of HCW observed	Before intervention: No.of opportunities	After intervention: No. of Observed sessions	After intervention: No.of HCW observed	After intervention: No.of opportunities	Overall: No. of Observed sessions	Overall: No.of HCW observed	Overall: No.of opportunities
41	Surg	no	27	17	61	311	992	13	49	144	74	360	1,136
42	Surg	no	28	20	65	302	946	9	34	78	74	336	1,024
43	Surg	no	21	30	47	258	625	27	112	324	74	370	949
44	Surg	no	22	28	63	312	756	11	49	117	74	361	873
45	Surg	no	26	51	45	247	600	29	128	327	74	375	927
46	Surg	no	27	37	44	211	540	30	128	358	74	339	898
47	Surg	no	25	47	63	329	872	11	44	128	74	373	1,000
48	Surg	yes	31	30	49	268	719	25	91	241	74	359	960
49	Surg	yes	32	22	64	313	1,030	9	36	91	73	349	1,121
50	Surg	yes	31	28	43	240	584	31	124	314	74	364	898

*Note: Obst= Obstetrics and gynecology; ENT= Ear Nose Throat; Paed= Paediatrics; Med=Medicine; Surg= Surgery

D.6: Summary of characteristics of all study wards (cont.)

Ward	Department*	ICU	No. of Permanent staff	No. of Visitors	Before intervention			After intervention			Overall		
					No. of Observed sessions	No.of HCW observed	No.of opportunities	No. of Observed sessions	No.of HCW observed	No.of opportunities	No. of Observed sessions	No.of HCW observed	No.of opportunities
51	Surg	yes	26	24	37	207	504	37	150	395	74	357	899
52	Surg	yes	32	9	47	271	601	26	104	272	73	375	873
53	Surg	yes	25	6	63	284	701	11	48	90	74	332	791
54	Surg	yes	30	28	63	324	925	11	36	150	74	360	1,075
56	Surg	yes	26	14	61	297	892	12	46	150	73	343	1,042
57	Surg	yes	23	9	62	296	826	12	59	131	74	355	957
58	Surg	no	25	22	44	229	578	30	121	364	74	350	942
Total			1,530	1,742	2,367	12,598	34,430	1,839	8,111	22,646	4,206	20,709	57,076

*Note: Obst= Obstetrics and gynecology; ENT= Ear Nose Throat; Paed= Paediatrics; Med=Medicine; Surg= Surgery

D.7: Hand hygiene compliance of study wards

Ward	Before intervention					After intervention					Overall					% Improvements		Per-protocol
	Obs	Mean	Std. Dev.	Min	Max	Obs	Mean	Std. Dev.	Min	Max	Obs	Mean	Std. Dev.	Min	Max			
1	269	4.46	5.78	0	20.00	665	9.32	13.31	0	80.00	934	7.92	11.86	0	80.00	4.86	↑↑	no
2	68	4.41	2.77	0	7.14	806	7.69	10.49	0	44.44	874	7.44	10.15	0	44.44	3.28	↑	yes
3	63	0.00	0.00	0	0.00	741	6.21	8.70	0	50.00	804	5.72	8.52	0	50.00	6.21	↑↑↑	yes
4	283	2.12	3.98	0	14.29	548	3.83	6.25	0	28.57	831	3.25	5.64	0	28.57	1.71	↑	yes
5	1,000	10.80	10.74	0	47.37	117	8.55	14.65	0	44.44	1,117	10.56	11.23	0	47.37	-2.25	↓	no
6	149	6.71	16.88	0	52.94	937	15.26	17.61	0	80.00	1,086	14.09	17.75	0	80.00	8.55	↑↑	yes
7	220	19.09	26.22	0	100.00	665	7.37	9.33	0	35.71	885	10.28	16.17	0	100.00	-11.72	↓	yes
8	184	5.43	7.80	0	23.08	671	5.81	8.15	0	30.00	855	5.73	8.07	0	30.00	0.38	↑	yes
9	139	13.67	17.59	0	50.00	778	11.44	16.05	0	83.33	917	11.78	16.30	0	83.33	-2.23	↓	yes
10	175	31.43	26.12	0	83.33	786	29.01	24.17	0	100.00	961	29.45	24.54	0	100.00	-2.42	↓	yes
11	243	8.23	13.61	0	58.33	585	13.85	18.23	0	100.00	828	12.20	17.19	0	100.00	5.62	↑	yes
12	707	29.56	21.22	0	90.00	61	39.34	13.59	20	60.00	768	30.34	20.88	0	90.00	9.78	↑	no
13	189	26.46	26.17	0	100.00	512	30.86	20.83	0	100.00	701	29.67	22.46	0	100.00	4.40	↑	yes
14	95	13.68	18.48	0	63.64	964	17.95	14.39	0	53.85	1,059	17.56	14.84	0	63.64	4.26	↑	yes
15	735	18.37	17.49	0	70.00	99	14.14	9.28	0	28.57	834	17.87	16.78	0	70.00	-4.23	↓	no

D.7: Hand hygiene compliance of study wards (cont.)

Ward	Before intervention					After intervention					Overall					% Improvements		Per-protocol
	Obs	Mean	Std. Dev.	Min	Max	Obs	Mean	Std. Dev.	Min	Max	Obs	Mean	Std. Dev.	Min	Max			
16	1,115	4.66	5.87	0	25.00	595	4.87	5.73	0	25.00	1,710	4.74	5.82	0	25.00	0.21	↑	yes
17	570	3.33	4.60	0	20.00	880	1.93	3.96	0	16.67	1,450	2.48	4.27	0	20.00	-1.40	↓	yes
18	1,276	5.88	8.38	0	45.00	86	2.33	4.01	0	10.00	1,362	5.65	8.22	0	45.00	-3.55	↓	yes
19	825	4.36	6.02	0	23.81	838	5.97	10.07	0	66.67	1,663	5.17	8.35	0	66.67	1.60	↑	yes
20	1,382	3.33	6.15	0	40.00	165	6.06	7.74	0	15.87	1,547	3.62	6.39	0	40.00	2.73	↑	no
21	967	3.31	4.72	0	28.57	558	7.35	8.18	0	33.33	1,525	4.79	6.51	0	33.33	4.04	↑↑	no
22	257	6.23	6.92	0	21.43	614	5.37	9.36	0	50.00	871	5.63	8.72	0	50.00	-0.85	↓	yes
23	531	16.95	17.23	0	91.67	437	9.15	12.31	0	66.67	968	13.43	15.69	0	91.67	-7.80	↓	yes
24	420	9.05	8.79	0	41.18	660	10.15	11.20	0	44.44	1,080	9.72	10.34	0	44.44	1.10	↑	yes
25	427	13.35	18.17	0	59.09	671	8.05	10.05	0	41.67	1,098	10.11	14.02	0	59.09	-5.30	↓	yes
26	354	13.28	16.61	0	64.29	646	9.44	10.29	0	45.45	1,000	10.80	13.00	0	64.29	-3.83	↓	yes
27	841	15.10	13.62	0	76.92	80	1.25	4.87	0	20.00	921	13.90	13.66	0	76.92	-13.85	↓	no
28	303	5.28	11.17	0	66.67	559	4.29	6.51	0	33.33	862	4.64	8.45	0	66.67	-0.99	↓	yes
29	790	8.73	9.48	0	40.00	67	13.43	15.97	0	40.00	857	9.10	10.20	0	40.00	4.70	↑	no
30	350	2.86	5.10	0	20.00	515	7.38	12.08	0	54.55	865	5.55	10.12	0	54.55	4.52	↑↑	no

D.7: Hand hygiene compliance of study wards (cont.)

Ward	Before intervention					After intervention					Overall					% Improvements		Per-protocol
	Obs	Mean	Std. Dev.	Min	Max	Obs	Mean	Std. Dev.	Min	Max	Obs	Mean	Std. Dev.	Min	Max			
31	663	12.97	14.34	0	62.50	78	5.13	15.27	0	50.00	741	12.15	14.63	0	62.50	-7.84	↓	yes
32	679	4.12	9.18	0	50.00	398	5.28	6.18	0	22.22	1,077	4.55	8.22	0	50.00	1.15	↑	yes
33	684	4.24	6.93	0	33.33	440	4.09	6.92	0	33.33	1,124	4.18	6.92	0	33.33	-0.15	↓	yes
34	887	7.10	13.63	0	76.92	82	4.88	9.33	0	25.00	969	6.91	13.33	0	76.92	-2.22	↓	no
35	569	10.54	9.92	0	33.33	363	6.34	10.53	0	50.00	932	8.91	10.36	0	50.00	-4.21	↓	yes
36	519	10.40	12.46	0	70.00	462	8.23	9.57	0	36.36	981	9.38	11.24	0	70.00	-2.18	↓	yes
37	487	7.80	10.72	0	54.55	496	10.28	15.04	0	56.25	983	9.05	13.13	0	56.25	2.48	↑	yes
38	634	7.10	10.62	0	50.00	125	13.60	16.40	0	54.55	759	8.17	12.00	0	54.55	6.50	↑	no
39	927	6.80	9.38	0	43.48	131	10.69	12.49	0	31.03	1,058	7.28	9.89	0	43.48	3.89	↑	no
40	763	3.15	6.30	0	28.57	91	0.00	0.00	0	0.00	854	2.81	6.03	0	28.57	-3.15	↓	no
41	992	8.97	11.51	0	50.00	144	4.86	7.60	0	20.00	1,136	8.45	11.17	0	50.00	-4.11	↓	yes
42	946	7.93	11.89	0	50.00	78	6.41	10.48	0	33.33	1,024	7.81	11.79	0	50.00	-1.52	↓	no
43	625	12.48	13.63	0	42.86	324	16.05	14.95	0	53.85	949	13.70	14.19	0	53.85	3.57	↑	yes
44	756	5.56	8.82	0	50.00	117	4.27	5.40	0	14.29	873	5.38	8.45	0	50.00	-1.28	↓	no
45	600	5.17	8.20	0	38.46	327	6.73	7.97	0	28.57	927	5.72	8.15	0	38.46	1.56	↑	yes

D.7: Hand hygiene compliance of study wards (cont.)

Ward	Before intervention					After intervention					Overall					% Improvements		Per-protocol
	Obs	Mean	Std. Dev.	Min	Max	Obs	Mean	Std. Dev.	Min	Max	Obs	Mean	Std. Dev.	Min	Max			
46	540	5.74	8.88	0	29.41	358	7.26	12.13	0	62.50	898	6.35	10.32	0	62.50	1.52	↑	yes
47	872	8.37	10.48	0	50.00	128	4.69	8.53	0	28.57	1,000	7.90	10.32	0	50.00	-3.68	↓	yes
48	719	17.80	14.96	0	60.00	241	14.52	13.66	0	50.00	960	16.98	14.71	0	60.00	-3.28	↓	yes
49	1,030	14.95	16.78	0	80.00	91	9.89	14.69	0	50.00	1,121	14.54	16.67	0	80.00	-5.06	↓	no
50	584	17.64	16.70	0	66.67	314	16.24	12.57	0	50.00	898	17.15	15.39	0	66.67	-1.39	↓	yes
51	504	18.45	20.62	0	78.57	395	19.75	14.40	0	66.67	899	19.02	18.15	0	78.57	1.29	↑	yes
52	601	20.13	19.96	0	78.95	272	18.38	18.79	0	75.00	873	19.59	19.61	0	78.95	-1.75	↓	yes
53	701	11.41	12.96	0	50.00	90	12.22	15.75	0	41.67	791	11.50	13.30	0	50.00	0.81	↑	no
54	925	11.57	15.36	0	68.75	150	8.67	13.65	0	44.44	1,075	11.16	15.16	0	68.75	-2.90	↓	no
56	892	15.70	15.97	0	75.00	150	29.33	23.28	0	87.50	1,042	17.66	17.85	0	87.50	13.64	↑	no
57	826	23.12	21.08	0	90.00	131	17.56	12.31	0	42.86	957	22.36	20.19	0	90.00	-5.57	↓	yes
58	578	4.84	6.11	0	20.00	364	10.16	9.50	0	33.33	942	6.90	8.03	0	33.33	5.32	↑↑	yes

D.8: Descriptive statistics for characteristics and covariates in the study by observed HCWs [*n*]

Variable	Before intervention (*n* = 11,112)	After intervention (*n* = 7,289)	Overall (*n* = 18,401)
Sex			
Male	2,934	1,537	4,471
Female	8,178	5,752	13,930
Type of HCWs			
Doctor	491	139	630
Registered Nurse	5,512	3,666	9,178
Technical Nurse	194	223	417
Nursing Assistant	473	314	787
Nursing Aide	2,382	1,527	3,909
Worker	1,177	1,053	2,230
Medical Student	118	29	147
Nursing Student	393	251	644
Visitor	372	87	459
Ward type			
Non-ICU wards	6,991	5,140	12,131
ICU wards	4,121	2,149	6,270
Department			
Obstetrics and gynecology	261	1,028	1,289
Eye	54	274	328
Ear Nose Throat	99	238	337
Pediatrics	1,193	1,623	2,816
Medicine	3,218	2,068	5,286
Surgery	6,287	2,058	8,345

D.9: Characteristic of hand hygiene compliance by the variables during before intervention

Variables	Before intervention (n = 34,430)						
	n	*Mean*	*SD*	Min	Max	Skewness	Kurtosis
Overall	34,430	10.10	20.85	0	100	2.61	10.01
Sex							
Male	7,837	5.33	15.16	0	100	3.78	19.43
Female	26,593	11.50	22.06	0	100	2.40	8.71
Type of HCW							
Doctor	1,829	5.41	15.09	0	100	3.37	15.53
Registered Nurse	18,702	14.56	24.38	0	100	2.06	6.86
Technical Nurse	588	12.41	22.36	0	100	2.18	7.66
Nursing Assistant	1,659	5.97	15.57	0	100	3.42	16.54
Nursing Aide	6,557	4.12	12.48	0	100	3.99	21.43
Worker	2,095	3.96	12.65	0	100	4.59	28.14
Medical Student	418	2.87	10.97	0	75	4.51	24.77
Nursing Student	1,361	5.44	15.52	0	100	3.55	17.32
Visitor	1,221	3.52	11.11	0	100	3.42	15.44

D.9: Characteristic of hand hygiene compliance by the variables during before intervention (cont.)

Variables	Before intervention (n = 34,430)						
	n	*Mean*	*SD*	Min	Max	Skewness	Kurtosis
Ward type							
Non-ICU wards	22,336	6.70	16.75	0	100	3.39	16.07
ICU wards	12,094	16.36	25.69	0	100	1.82	5.73
Department							
Obstetrics and gynecology	683	3.07	10.36	0	100	4.73	31.81
Eye	175	31.43	40.86	0	100	0.83	1.93
Ear Nose Throat	243	8.23	22.02	0	100	2.95	11.01
Pediatrics	3,418	17.44	26.98	0	100	1.70	5.15
Medicine	11,071	7.37	17.22	0	100	3.06	13.48
Surgery	18,840	10.45	21.04	0	100	2.58	9.85
Indication for performing hand hygiene							
Before touching a patient	7,904	7.53	17.03	0	100	3.01	13.30
After touching a patient	7,781	7.67	17.32	0	100	2.99	13.07
Before clean/aseptic procedures	4,266	18.93	28.68	0	100	1.63	4.74
After body fluid exposure/risk	4,780	17.67	28.16	0	100	1.72	5.05
After touching patient surroundings	9,699	6.52	15.14	0	100	3.12	14.82

D.10: Characteristic of hand hygiene compliance by the variables and during after intervention

Variables	After intervention (n = 22,646)						
	n	*Mean*	*SD*	Min	Max	Skew	Kurtosis
Overall	22,646	10.33	19.92	0	100	2.31	8.37
Sex							
Male	3,874	7.80	18.66	0	100	2.89	11.57
Female	18,772	10.85	20.14	0	100	2.22	7.91
Type of HCW							
Doctor	609	8.21	18.33	0	100	2.52	9.55
Registered Nurse	12,667	13.14	21.83	0	100	1.91	6.37
Technical Nurse	506	11.86	22.85	0	100	2.24	7.62
Nursing Assistant	1,233	8.11	17.65	0	100	2.86	12.05
Nursing Aide	4,306	6.90	17.26	0	100	3.25	14.32
Worker	1,816	5.23	13.11	0	100	3.18	14.57
Medical Student	101	0.99	7.00	0	50	6.89	48.52
Nursing Student	1,084	4.43	12.38	0	75	3.16	13.11
Visitor	324	7.41	15.87	0	60	2.08	6.12

D.10: Characteristic of hand hygiene compliance by the variables and during after intervention (cont.)

Variables	After intervention (n = 22,646)						
	n	*Mean*	*SD*	Min	Max	Skew	Kurtosis
Ward type							
Non-ICU wards	16,089	8.65	18.90	0	100	2.73	10.80
ICU wards	6,557	14.46	21.69	0	100	1.61	5.18
Department							
Obstetrics and gynecology	2,760	6.92	16.15	0	100	3.21	14.94
Eye	786	29.01	34.91	0	100	0.90	2.34
Ear Nose Throat	585	13.85	23.31	0	100	1.97	6.61
Pediatrics	4,804	14.55	23.21	0	100	1.68	5.21
Medicine	7,449	6.44	14.61	0	100	2.74	11.28
Surgery	6,262	10.54	19.20	0	100	2.20	7.97
Indication for performing hand hygiene							
Before touching a patient	4,802	9.31	18.74	0	100	2.45	9.20
After touching a patient	4,697	9.28	18.72	0	100	2.46	9.23
Before clean/aseptic procedures	2,604	17.20	24.92	0	100	1.55	4.71
After body fluid exposure/risk	2,668	16.86	24.77	0	100	1.57	4.78
After touching patient surroundings	7,875	7.09	16.23	0	100	2.94	12.97

D.11: Characteristic of hand hygiene compliance by the variables during overall intervention

Variables	Overall intervention (n = 57,076)						
	n	*Mean*	*SD*	Min	Max	Skew	Kurtosis
Overall	57,076	10.19	20.49	0	100	2.51	9.44
Sex							
Male	11,711	6.15	16.44	0	100	3.43	15.95
Female	45,365	11.23	21.29	0	100	2.35	8.53
Type of HCW							
Doctor	2,438	6.11	16.01	0	100	3.11	13.47
Registered Nurse	31,369	13.99	23.39	0	100	2.02	6.83
Technical Nurse	1,094	12.16	22.57	0	100	2.21	7.64
Nursing Assistant	2,892	6.88	16.52	0	100	3.16	14.28
Nursing Aide	10,863	5.22	14.63	0	100	3.71	18.44
Worker	3,911	4.55	12.88	0	100	3.89	21.20
Medical Student	519	2.50	10.34	0	75	4.81	27.60
Nursing Student	2,445	4.99	14.22	0	100	3.51	17.19
Visitor	1,545	4.34	12.36	0	100	3.02	11.99
Ward type							
Non-ICU wards	38,425	7.52	17.70	0	100	3.08	13.41
ICU wards	18,651	15.69	24.37	0	100	1.79	5.80

D.11: Characteristic of hand hygiene compliance by the variables during overall intervention (cont.)

Variables	Overall intervention (n = 57,076)						
	n	*Mean*	*SD*	Min	Max	Skew	Kurtosis
Department							
Obstetrics and gynecology	3,443	6.16	15.26	0	100	3.42	16.79
Eye	961	29.45	36.06	0	100	0.90	2.28
Ear Nose Throat	828	12.20	23.07	0	100	2.20	7.50
Pediatrics	8,222	15.75	24.89	0	100	1.72	5.37
Medicine	18,520	7.00	16.23	0	100	3.00	13.30
Surgery	25,102	10.47	20.59	0	100	2.51	9.55
Indication for performing hand hygiene							
Before touching a patient	12,706	8.20	17.71	0	100	2.77	11.45
After touching a patient	12,478	8.27	17.87	0	100	2.77	11.38
Before clean/aseptic procedures	6,870	18.28	27.33	0	100	1.63	4.85
After body fluid exposure/risk	7,448	17.38	26.99	0	100	1.69	5.07
After touching patient surroundings	17,574	6.78	15.64	0	100	3.04	13.94

D.12: Compliance with hand hygiene at before and at after intervention

	Before intervention			After intervention			
	No. of HH events	No. of HH opportunities	Compliance (%)	No. of HH events	No. of HH opportunities	Compliance (%)	*P* value
Overall	8,013	34,430	10.10	4,943	22,646	10.33	
Sex							
Male	1,917	7,837	5.33	886	3,874	7.80	
Female	6,096	26,593	11.50	4,057	18,772	10.85	
Type of HCW							
Doctor	497	1,829	5.41	140	609	8.21	
Registered Nurse	4,244	18,702	14.56	2,702	12,667	13.14	
Technical Nurse	147	588	12.41	139	506	11.86	
Nursing Assistant	335	1,659	5.97	230	1,233	8.11	
Nursing Aide	1,387	6,557	4.12	904	4,306	6.90	
Worker	523	2,095	3.96	461	1,816	5.23	
Medical Student	118	418	2.87	29	101	0.99	
Nursing Student	393	1,361	5.44	251	1,084	4.43	
Visitor	370	1,221	3.52	87	324	7.41	

D.12: Compliance with hand hygiene at before and at after intervention (cont.)

	Before intervention			After intervention			
	No. of HH events	No. of HH opportunities	Compliance (%)	No. of HH events	No. of HH opportunities	Compliance (%)	*P* value
Ward type							
Non-ICU wards	5,032	22,336	6.70	3,468	16,089	8.65	
ICU wards	2,981	12,094	16.36	1,475	6,557	14.46	
Department							
Obstetrics and gynecology	176	683	3.07	652	2,760	6.92	
Eye	35	175	31.43	163	786	29.01	
Ear Nose Throat	65	243	8.23	136	585	13.85	
Pediatrics	873	3,418	17.44	1,134	4,804	14.55	
Medicine	2,478	11,071	7.37	1,508	7,449	6.44	
Surgery	4,386	18,840	10.45	1,350	6,262	10.54	
Indication for performing hand hygiene							
Before touching a patient		7,904	7.53		4,802	9.31	
After touching a patient		7,781	7.67		4,697	9.28	
Before clean/aseptic procedures		4,266	18.93		2,604	17.20	
After body fluid exposure/risk		4,780	17.67		2,668	16.86	
After touching patient surroundings		9,699	6.52		7,875	7.09	

Appendix E

Publications arising directly from the thesis

PLOS | ONE

Increasing Incidence of Hospital-Acquired and Healthcare-Associated Bacteremia in Northeast Thailand: A Multicenter Surveillance Study

Maliwan Hongsuwan[1], Pramot Srisamang[2], Manas Kanoksil[3], Nantasit Luangasanatip[1], Anchalee Jatapai[1], Nicholas P. Day[1,4], Sharon J. Peacock[1,5,6], Ben S. Cooper[1,4], Direk Limmathurotsakul[1,7]*

1 Mahidol-Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand, 2 Department of pediatrics, Sappasithiprasong Hospital, Ubon Ratchathani, Thailand, 3 Department of pediatrics, Udon Thani Hospital, Udon Thani, Thailand, 4 Center for Tropical Medicine, Nuffield Department of Clinical Medicine, University of Oxford, Oxford, United Kingdom, 5 Department of Microbiology and Immunology, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand, 6 Department of Medicine, Cambridge University, Addenbrooke's Hospital, Cambridge, United Kingdom, 7 Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

Abstract

Background: Little is known about the epidemiology of nosocomial bloodstream infections in public hospitals in developing countries. We evaluated trends in incidence of hospital-acquired bacteremia (HAB) and healthcare-associated bacteremia (HCAB) and associated mortality in a developing country using routinely available databases.

Methods: Information from the microbiology and hospital databases of 10 provincial hospitals in northeast Thailand was linked with the national death registry for 2004–2010. Bacteremia was considered hospital-acquired if detected after the first two days of hospital admission, and healthcare-associated if detected within two days of hospital admission with a prior inpatient episode in the preceding 30 days.

Results: A total of 3,424 patients out of 1,069,443 at risk developed HAB and 2,184 out of 119,286 at risk had HCAB. Of these 1,559 (45.5%) and 913 (41.8%) died within 30 days, respectively. Between 2004 and 2010, the incidence rate of HAB increased from 0.6 to 0.8 per 1,000 patient-days at risk ($p<0.001$), and the cumulative incidence of HCAB increased from 1.2 to 2.0 per 100 readmissions ($p<0.001$). The most common causes of HAB were *Acinetobacter* spp. (16.2%), *Klebsiella pneumoniae* (13.9%), and *Staphylococcus aureus* (13.9%), while those of HCAB were *Escherichia coli* (26.3%), *S. aureus* (14.0%), and *K. pneumoniae* (9.7%). There was an overall increase over time in the proportions of ESBL-producing *E. coli* causing HAB and HCAB.

Conclusions: This study demonstrates a high and increasing incidence of HAB and HCAB in provincial hospitals in northeast Thailand, increasing proportions of ESBL-producing isolates, and very high associated mortality.

Citation: Hongsuwan M, Srisamang P, Kanoksil M, Luangasanatip N, Jatapai A, et al. (2014) Increasing Incidence of Hospital-Acquired and Healthcare-Associated Bacteremia in Northeast Thailand: A Multicenter Surveillance Study. PLoS ONE 9(10): e109324. doi:10.1371/journal.pone.0109324

Editor: Linda Anne Selvey, Curtin University, Australia

Received May 21, 2014; **Accepted** August 31, 2014; **Published** October 13, 2014

Data Availability: The authors confirm that, for approved reasons, some access restrictions apply to the data underlying the findings. Data used in the study are held by the Ministry of Public Health, Thailand, and are not open access based on the need on patient confidentiality. I confirm that other researchers will be able to obtain all data from the Ministry in the same manner that we do. After ethical approval from the ethical committee of Ministry of Public Health, the requests could be done through Director of each hospital participating in the study.

Funding: The work was supported by the Wellcome Trust of Great Britain (grant number 089275/Z/09/Z). BSC was supported by The Medical Research Council and Department for International Development (grant number MR/K006924/1). SJP receives support from the NIHR Cambridge Biomedical Research Centre. DL is supported by an Intermediate Wellcome Trust Fellowship (grant number 101103/Z/13/Z). The funder has no role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing Interests: The authors have declared that no competing interests exist.

* Email: direk@tropmedres.ac

Introduction

Nosocomial infections are the most frequent adverse event in healthcare delivery worldwide, but there is a paucity of information about their epidemiology from developing countries [1]. This is particularly true for nosocomial bacteremia which are frequently used as indicators of trends in overall nosocomial infection in developed countries because of the availability of clear definitions and clinical relevance [2,3]. A recent comprehensive systematic review found only 13 studies of bloodstream infection from developing countries between 1995 and 2008, with only six studies in the Southeast Asia region and none from the Western Pacific region [1]. For example, the reported incidence rates of hospital-acquired bacteremia (HAB) through active surveillance were 1.0 per 1,000 patient-days in a district hospital in Kenya between 2002–2009 [4], and 1.2 per 1,000 patient-days in a university hospital in Iran in 2006 [5]. This lack of information is a consequence, at least in part, of the paucity of reliable surveillance systems for such outcomes in resource-limited settings. Moreover, published literature from developing countries is often from better resourced or university hospitals [4,5], and may not provide a reliable basis for generalization to public hospitals in those countries.

In this study, we combined multiple sources of routine surveillance data including microbiology databases, hospital admission databases and the national death registry from a sample of provincial hospitals in northeast Thailand [6]. Our objectives were to demonstrate trends in incidence, antibiotic-resistance and mortality associated with HAB and healthcare-associated bacteremia (HCAB) over a seven year period.

Materials and Methods

Study population

Northeast Thailand consists of 20 provinces, covers 170,226 km^2 and had an estimated population in 2010 of 21.4 million. Each province has a provincial hospital that provides care to people living within its catchment area and acts as a referral hospital for smaller district hospitals. The number of beds per provincial hospital ranges from 200 to 1000, and all provincial hospitals are equipped with intensive care units (ICUs). Severely ill patients presenting to district hospitals are often referred to provincial hospitals. Provincial hospitals are equipped with a microbiology laboratory that provides a bacterial culture service, while district hospitals normally do not have such facilities. All microbiology laboratories in provincial hospitals use standard methodologies for bacterial identification and susceptibility testing provided by the Bureau of Laboratory Quality and Standards, Ministry of Public Health, Thailand [7].

Study design

We conducted a retrospective, multicenter surveillance study of all provincial hospitals in northeast Thailand. The data were collected as previously described [2]. In brief, the director of each hospital was contacted and given information on the study. For those hospitals that agreed to participate, data were collected from the microbiology and hospital databases between Jan 2004 to Dec 2010. Admission number (AN) was used as the record linkage between the two databases, and hospital number (HN) was used to identify individuals who had repeated admissions. The death registry for northeast Thailand between Jan 2004 to Jan 2011 was obtained from the Ministry of Interior, Thailand, and used to identify patients who were discharged from hospital and died within 30 days after discharge from the hospital. Ethical permission for this study was obtained from the Ethical and Scientific Review Committees of Faculty of Tropical Medicine, Mahidol University, and of the Ministry of Public Health, Thailand. Written consent was given by the director of the hospitals to use the routine hospital database for research. Consent was not sought from the patients as this was a retrospective study, and the Ethical and Scientific Review Committees approved the process.

Data collection

The microbiology laboratory data collected were HN, AN, specimen type, specimen date, culture result, and antibiotic susceptibility profile (antibiogram). Hospital data were collected from the routine in-patient discharge report (Report 501), which is regularly completed by attending physicians and reported to the Ministry of Public Health, Thailand, as part of national morbidity and mortality reporting system. The data collected were HN, AN, national identification 13-digit number, gender, age, admission date, discharge date, and outcome. A single outcome variable is required by this reporting system, which is completed by the attending physicians and categorized as cured, improved, not improved, transfer to another hospital, refusal of treatment, or died. Date of death was also extracted from this record. Data collected from the death registry obtained from the Ministry of Interior were national identification 13-digit number and date of death. Data are not suitable for public deposition due to ethical restrictions. Raw database requests may be made to the director of each participating hospital (Table S1).

Definitions

Bacteremia was classified as community-acquired bacteremia (CAB), HAB or HCAB. CAB was defined as the isolation of a pathogenic organism from blood taken in the first 2 days of admission and without a hospital stay in the 30 days prior to admission [2]. HAB was defined as the isolation of a pathogenic organism from blood taken after the first 2 days of admission [8,9]. HCAB was defined as the isolation of a pathogenic organism from blood taken in the first 2 days of admission and with a hospital stay within 30 days prior to the admission [8,9]. Patients at risk of HCAB were those with a hospital stay within 30 days prior to the admission. Patients were considered at risk of HAB after they stayed in the hospital for more than 2 days. Because of the difficulty in establishing their clinical significance, organisms frequently associated with contamination including coagulase-negative *staphylococc*i, viridans group *streptococci*, *Corynebacterium* spp., *Bacillus* spp., *Diptheroid* spp., *Micrococcus* spp., and *Propionibacterium* spp. were excluded from the analysis [10]. Organisms that produced an extended-spectrum β lactamase (ESBL) were defined using standard methodologies for bacterial identification and susceptibility testing provided by the Bureau of Laboratory Quality and Standards, Ministry of Public Health, Thailand [7]. All patients with bacteremia caused by *B. pseudomallei* were categorized as CAB because this organism is not a cause of HAB or HCAB [11]. Polymicrobial infection was defined in patients who had more than one species of pathogenic organisms isolated from the blood during the same episode. Information on patients with a first CAB episode has been published previously [2]. In this study, patients with a first episode of HAB or HCAB were evaluated in relation to epidemiology and mortality.

The 30-day mortality of HAB was determined on the basis of a record of death within 30 days of the positive blood culture taken as recorded in the routine hospital database or by a record of death in the national death registry. The 30-day mortality of HCAB was defined as death within 30 days of the admission date. The incidence rate of HAB was calculated as the number of HAB per 1,000 patient-days at risk. The cumulative incidence of HCAB was calculated as the number of HCAB per 100 readmissions. To avoid the assessment of multiple outcomes for a single patient, in the event that a patient had more than one episode of bacteremia (either HAB and/or HCAB) only the first episode was included in the study.

Statistical analysis

All analyses were performed using STATA version 12.0 (StataCorp LP, College station, Texas). Poisson regression models were used to calculated incidence rate ratios, and logistic regression models were used to calculated odds ratios. Fisher's exact test was used to compare categorical variables. The Mann-Whitney test was used to compare continuous variables. A non-parametric test for trend was used to assess change in proportion over time and stratified by hospital (using the npt_s command in STATA).

Results

All 20 provincial hospitals in northeast Thailand were contacted to participate in this study. Agreement was obtained from 15 (75%) hospitals, of which 10 had microbiological laboratory and hospital databases as electronic files in a readily accessible format (Figure S1). Of the 10 hospitals included in the analysis, 3 (30%) had data available for the period 2004–2010, 1 (10%) between 2006–2010, 2 (20%) between 2007–2010, 3 (30%) between 2008–2010, and 1 (10%) between 2009–2010 (Tables 1 and 2). The median bed number was 450 beds (range 300 to 1,000 beds). A total of 1,969,474 admission records from 1,372,446 patients were evaluated, of which 21,438 (1.1%) admission records had at least one blood culture positive for pathogenic organisms during admission. A total of 3,451 (16.1%) episodes were defined as hospital-acquired bacteremia (HAB), 2,302 (10.7%) episodes were healthcare-associated bacteremia (HCAB) and 15,685 (73.2%) episodes were community-acquired bacteremia (CAB). Multiple episodes of HAB and HCAB were noted in 26 and 102 patients, respectively. Only the first episodes of HAB and HCAB in 3,424 and 2,184 patients, respectively, were included in further analysis.

Incidence of HAB and HCAB

The average incidence rate for HAB during the 7-year study period was 0.7 per 1,000 patient-days, with an overall increase in rate over time. The incidence rate of HAB increased from 0.6 in 2004 to 0.8 per 1,000 patient-days in 2010 ($p<0.001$) (Table 1).

Of 1,969,474 admission records, 119,286 (10.1%) had a hospital stay within 30 days prior to admission and were at risk of HCAB. The cumulative incidence for HCAB during the 7-year study period was 1.8 per 100 readmissions, with an overall increase in the cumulative incidence over time. The cumulative incidence of HCAB increased from 1.2 in 2004 to 2.0 per 100 readmissions in 2010 ($p<0.001$) (Table 2). The incidence rate of HAB and HCAB varied by hospitals (Figure S2 and S3), but the overall increasing trends were observed in most hospitals.

Demographic risk factors for HAB and HCAB

Of 3,424 patients with a primary episode of HAB, 2,000 (58.4%) were male and 1,424 (41.6%) were female. The median age was 51 years (interquartile range [IQR] 16–67 years, range 0–88 years). The median time from hospital admission to bacteremia was 8 days (IQR 4–15 days, range 3–105 days). The median length of stay for patients with HAB was longer than patients who were at risk of, but did not develop HAB (18 vs. 4 days, $p<0.001$). The overall incidence rate of HAB was higher in males than in females (0.8 vs. 0.6 per 1,000 patient-days, incidence rate ratio [IRR] 1.21; 95% confidence interval [CI] 1.13 to 1.30, $p<0.001$) (Figure 1). The incidence rates of HAB were highest in infants (1.1 per 1,000 patient-days), and in those older than 80 years of age (0.9 per 1,000 patient-days).

Of 2,184 patients with a primary episode of HCAB, 1,166 (53.4%) were male and 1,018 (46.6%) were female. Median age was 57 years (IQR 41–70 years, range 0–89 years). The median time between prior and study admission was 11 days (IQR 6–19 days, range 1–30 days). The median length of stay for patients with HCAB was longer than patients who were at risk of, but did not present with HCAB (6 vs. 3 days, $p<0.001$). Male gender was associated with a higher risk of HCAB (odds ratio [OR] 1.29; 95%CI 1.18 to 1.40, $p<0.001$) (Figure 2). The incidence rates of

Table 1. Incidence rates of hospital-acquired bacteremia (HAB) and associated death rate between 2004 and 2010 in northeast Thailand.

Year	Total number of hospitals with available data	Total number of hospital admissions	Total number of hospital admissions at risk of HAB*	Total number of patients with HAB	Deaths associated with HAB	30-day mortality associated with HAB	Incidence rate for HAB (per 1,000 patient-days)
2004	3	129,376	74,272	212	90	42.5%	0.6
2005	3	138,816	79,254	292	120	41.1%	0.8
2006	4	187,812	102,948	259	100	38.6%	0.5
2007	6	241,208	129,574	366	185	50.5%	0.6
2008	9	372,564	199,154	640	281	43.9%	0.7
2009	10	453,791	239,814	840	388	46.2%	0.8
2010	10	445,907	244,427	815	395	48.5%	0.8
Overall	10	1,969,474	1,069,443	3,424	1,559	45.5%	0.7

*Patients at risk of HAB were patients who stayed in the hospital longer than 2 days.

doi:10.1371/journal.pone.0109324.t001

Table 2. Cumulative incidence of healthcare-associated bacteremia (HCAB) and associated death rate between 2004 and 2010 in northeast Thailand.

Year	Total number of hospitals with available data	Total number of hospital admissions	Total number of hospital admission at risk of HCAB*	Total number of patients with HCAB	Deaths associated with HCAB	30-day mortality associated with HCAB	Cumulative incidence for HCAB (per 100 readmissions)
2004	3	129,376	7,259	86	44	51.2%	1.2
2005	3	138,816	8,266	125	41	32.8%	1.5
2006	4	187,812	10,960	157	68	43.3%	1.4
2007	6	241,209	14,234	272	117	43.0%	1.9
2008	9	372,564	22,601	435	198	45.5%	1.9
2009	10	453,790	26,969	527	206	39.1%	2.0
2010	10	445,907	28,997	582	239	41.1%	2.0
Overall	10	1,969,474	119,286	2,184	913	41.8%	1.8

*Patients at risk of HCAB were patients who had a hospital stay within 30 days prior to the admission.
doi:10.1371/journal.pone.0109324.t002

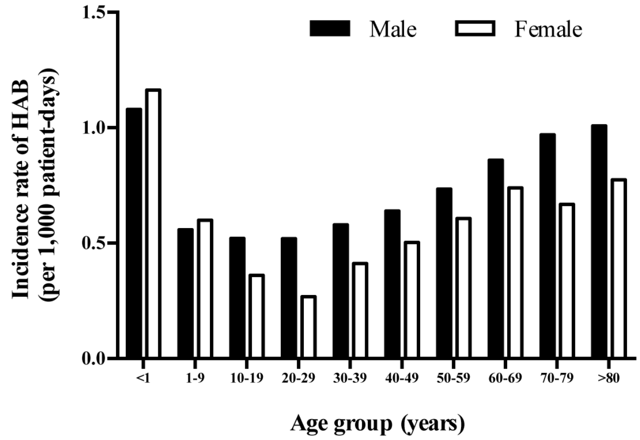


Figure 1. Age- and gender- specific incidence rates of hospital-acquired bacteremia (HAB) between 2004 and 2010 in northeast Thailand.
doi:10.1371/journal.pone.0109324.g001

HCAB were high in infants (1.1 per 100 readmission), and very high in those older than 30 years of age (Figure 2).

Pathogenic organisms associated with HAB and HCAB

Of all pathogenic organisms causing HAB, 2,313 (67.6%) were Gram-negative bacteria, 885 (25.8%) were Gram-positive bacteria, 81 (2.4%) were fungi, 3 (0.1%) were *Mycobacterium* spp., and 141 (4.1%) were polymicrobial (Table 3). The most common pathogens identified were *Acinetobacter* spp. (16.2%), *Klebsiella pneumoniae* (13.9%), *Staphylococcus aureus* (13.9%), *Escherichia coli* (12.6%), and *Pseudomonas* spp. (10.5%). Amongst *S. aureus* HABs, the proportion of methicillin-resistant *S. aureus* (MRSA) was 37.0% (176/476). Corresponding proportions of extended-spectrum β lactamase (ESBL)-producing *E. coli* and *K. pneumoniae* were 38.9% (169/434) and 59.3% (283/477), respectively.

Of all pathogenic organisms causing HCAB, 1,470 (67.3%) were Gram-negative bacteria, 592 (27.1%) were Gram-positive bacteria, 24 (1.1%) were fungi, 4 (0.2%) were *Mycobacterium* spp., and 94 (4.3%) were polymicrobial (Table 3). The most common pathogens identified were *E. coli* (26.3%), *S. aureus* (14.0%), *K. pneumoniae* (9.7%), *Pseudomonas* spp. (9.4%) and *Acinetobacter* spp. (5.7%). The proportion of ESBL-producing *E. coli,* ESBL-

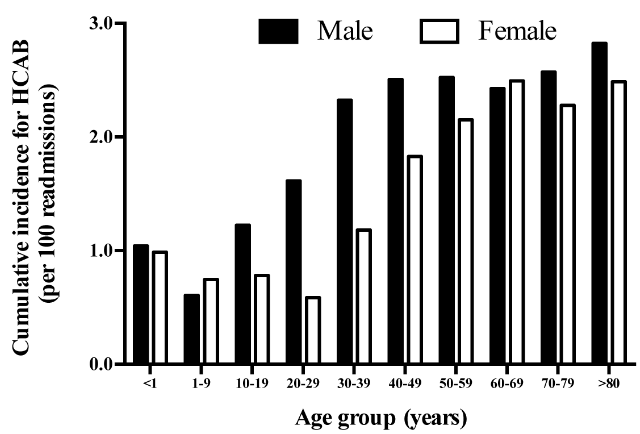


Figure 2. Age- and gender- specific cumulative incidence rates of healthcare-associated bacteremia (HCAB) between 2004 and 2010 in northeast Thailand.
doi:10.1371/journal.pone.0109324.g002

Table 3. Pathogenic organisms associated with hospital-acquired bacteremia (HAB) or healthcare-acquired bacteremia (HCAB).

Organisms	HAB	HCAB
Gram negative bacteria	2,313 (67.6%)	1,470 (67.3%)
Acinetobacter spp.	554 (16.2%)	124 (5.7%)
Escherichia coli		
ESBL –ve	265 (7.7%)	400 (18.3%)
ESBL +ve	169 (4.9%)	175 (8.0%)
Klebsiella pneumoniae		
ESBL –ve	194 (5.7%)	141 (6.5%)
ESBL +ve	283 (8.3%)	70 (3.2%)
Klebsiella spp.	122 (3.6%)	55 (2.5%)
Enterobacter spp.	155 (4.5%)	44 (2.0%)
Pseudomonas spp.	358 (10.5%)	205 (9.4%)
Other Gram-negative bacteria	213 (6.2%)	256 (11.7%)
Gram positive bacteria	885 (25.8%)	592 (27.1%)
Staphylococcus aureus		
Methicillin-susceptible	300 (8.8%)	231 (10.6%)
Methicillin-resistant	176 (5.1%)	74 (3.4%)
Enterococcus spp.	173 (5.1%)	74 (3.4%)
Other Gram positive bacteria	236 (6.9%)	213 (9.8%)
Fungi	81 (2.4%)	24 (1.1%)
Cryptococcus spp.	16 (0.5%)	20 (0.9%)
Candida spp.	59 (1.7%)	4 (0.2%)
Penicillium spp.	6 (0.2%)	–
Histoplasma spp.	1 (0.0%)	–
Mycobacterium spp.	3 (0.1%)	4 (0.2%)
Polymicrobial infection	141 (4.1%)	94 (4.3%)
Overall	3,424 (100.0%)	2,184 (100.0%)

doi:10.1371/journal.pone.0109324.t003

producing *K. pneumoniae* and MRSA were 30.4% (175/575), 33.2% (70/211), and 24.3% (74/305), respectively.

There were no differences in the patterns of common pathogens identified among different provinces or over the study period. However, there was an overall increase in the proportions of ESBL-producing *E. coli* over time. From 2004 to 2010, the proportion of ESBL-producing *E. coli* causing HAB rose from 33.3% (10/30) to 51.5% (51/99) ($p = 0.005$), and that causing HCAB rose from 20.8% (5/24) to 32.9% (48/146) ($p < 0.001$). The rising trend of ESBL-producing *E. coli* was observed in most hospitals. We did not observe a clear overall trend in the proportions of ESBL-producing *K. pneumoniae* or MRSA.

Mortality associated with HAB and HCAB

Death within 30-days of the positive blood culture taken was identified in 1,559 patients with HAB, giving an overall 30-day mortality of 45.5% (Table 1). Considering all patients who were admitted for more than 2 days, the 30-day mortality of those with HAB was higher than those without HAB (45.5% [1,559/3,424] vs. 5.5% [45,807/833,818], $p < 0.001$). Death in HAB patients occurred rapidly, with 749 of 1,559 deaths (48.0%) occurring within two days of the bacteremia, 89 (5.7%) on day 3, and 74 (4.8%) on day 4. Death in HAB patients occurred in hospital in 58.4% (911/1,559) of cases, the reminder occurring after hospital discharge. There was no change in the 30-day mortality associated with HAB over time ($p = 0.58$).

Death within 30 days of admission with an episode of HCAB was identified in 913 patients, giving an overall 30-day mortality of 41.8% (Table 2). Considering all patients who had a hospital stay within 30 days prior to the admission, the mortality of those with HCAB was significantly higher than those without HCAB (41.8% [913/2,184] vs. 13.0% [15,168/117,102], $p < 0.001$). Death in HCAB patients also occurred rapidly, with 410 of 913 deaths (45.7%) occurring within the first two days of admission, 54 (6.0%) on day 3, and 46 (5.1%) on day 4. Death in HCAB patients occurred in hospital in 43.2% (394/913) of cases, the reminder occurring after hospital discharge. There was no change in the 30-day mortality associated with HCAB over time ($p = 0.36$).

Discussion

Our study showed that nosocomial infection is an increasing and important problem in northeast Thailand. The total number of deaths associated with HAB and HCAB in 2010 in our study ($n = 634$) were much higher than the total number of reported deaths due to important notifiable diseases such as dengue hemorrhagic fever ($n = 139$), influenza ($n = 126$), and leptospirosis ($n = 43$) during the same period countrywide [12]. There was a 32.3% increase in the incidence rate of HAB and 66.8% in the cumulative incidence of HCAB between 2004 and 2010 in northeast Thailand. These estimates reinforce the need for improved surveillance and prevention of nosocomial infection in developing countries.

An incidence rate of HAB in the participating hospitals in 2010 of 0.8 per 1,000 patient-days is higher than recent estimates in high-income countries, including 0.7 per 1,000 patient-days in Canada between 2007–2010 [13], 0.6 per 1,000 patient-days in the USA in 2005 [14], and 0.6 per 1,000 patient-days in Estonia between 2004–2005 [15]. The Thai data are consistent with a recent review showing that other parameters used to estimate the burden of nosocomial infection in developing countries, such as prevalence of healthcare associated infections and ICU-acquired infections, are substantially higher than in developed countries [1]. The recent surveillance study conducted by the International Nosocomial Infection Control Consortium (INICC) also found that rates of central line associated bloodstream infection (CLAB) were significantly higher in ICUs in developing countries (6.8 per 1,000 central line-days) versus those reported in US ICUs (2.0 per 1,000 central line-days) [16]. Our HAB incidence rate is, however, lower than HAB rates reported through active surveillance in some developing countries, including 1.0 per 1,000 patient-days in Kenya between 2002–2009 [4], and 1.2 per 1,000 patient-days in Iran in 2006 [5]. It is possible that active surveillance may improve the detection of HAB and nosocomial infection in our geographical region.

During the study period, *Acinetobacter* spp. was the most common pathogen associated with HAB, followed by *K. pneumoniae* and *S. aureus*. *Acinetobacter* spp. is increasingly recognized as an important cause of nosocomial infection [17], and our study confirms the importance this species as a leading cause of nosocomial infection in developing tropical countries [1,4,18]. The proportion of MRSA causing HAB in our setting (37%) was higher than that reported from developed countries [13,15,19], and is consistent with a previous review of developing countries [1]. An increase in the proportion of ESBL-producing *E. coli* causing HAB in our study is alarming, and is consistent with our previous report of an increase in the proportion of ESBL-producing organisms causing CAB in the same setting [6].

This study highlights an increasing incidence of HCAB in developing countries. We used the total number of patients with readmission as a denominator to estimate the cumulative incidence of HCAB rather than the total number of patients with bacteremia [8,9,20]. Our estimates showed that healthcare-associated infection was an increasing cause of readmission. The high proportion of MRSA, ESBL-producing *E. coli* and ESBL-producing *K. pneumoniae* amongst organisms causing HCAB was relatively similar to that causing HAB. Much lower resistance levels were seen in organisms causing CAB [6]. This is consistent with previous reports of HCAB in developed countries [8,9,20].

The observed increase in incidence of both HAB and HCAB could be due to a combination of an increase in the incidence of nosocomial infection associated with a rise in the number of at-risk patients (for example aging patients and those with invasive interventions), and an increase in detection of HAB and HCAB due to improved healthcare practice over time. There is evidence that the incidence rate of CLAB in developing countries can be substantially reduced using a multi-dimensional infection control approach including a bundle of interventions, education, outcome surveillance, process surveillance, feedback on CLAB rate and performance feedback [21–27].

The overall 30-day mortality with HAB of 45.5% in our setting is much higher than that typically reported in high-income countries [13,15,28], but lower than the reported in-hospital mortality of 53% from a rural district hospital in Kenya [4]. The overall 30-day mortality with HCAB of 41.8% in our setting is also much higher than typically seen in high-income countries [8,9,20]. In addition to patient-related factors, the higher mortality typically seen in developing countries may be related to the proportion of antimicrobial-resistant pathogens, empirical antibiotic regimens used, and sub-optimal severe sepsis management in resource-limited settings [4,29]. It is also possible that practice in high-income countries can detect milder bacteremia cases such as cases due to intravenous device that is then rapidly removed, while the practice in low-income countries may be less likely to achieve this. The high mortality observed in our study also reflects post-dischage ascertainment of patient outcomes using the national death registry. We found that in 47.2% of fatal cases of HAB or HCAB death occurred after hospital discharge. This reflects a preference amongst people in the study area to die at home. Further studies need to explore how to reduce the mortality of patients with HAB and HCAB in resource-limited areas.

A limitation of this study is that more complete clinical data were not available. As data on central line days were not available, the incidence rate of CLAB per 1,000 central line days could not be estimated and benchmarked against other prospective studies [30–47]. As data on process surveillance were not available, the reasons for the increased incidence of HAB could not be systematically assessed [32,41,48,49]. Another potential limitation is that blood cultures may not have been performed for all patients with a likelihood of nosocomial infection, and this might lead to an underestimation in the incidence of HAB and HCAB among participating hospitals. In addition, data on hospitalization in other hospitals not participating in the study (for example, a district hospital or a private hospital in the province) were not available, which could have resulted in an underestimation of the incidence of HAB and HCAB in our study. It is also possible that some patients with HAB and HCAB in our study may have had contaminated cultures and were incorrectly counted. However, the high mortality in patients with HAB and HCAB suggested that true infection was more likely than culture contamination. Although our data showed that, in general, patients with HAB and HCAB stayed in the hospital longer than those without, the analysis did not take account of the high mortality associated with HAB and HCAB. The length of stay would be further extended if death of patients with HAB and HCAB could be reduced. Additional costs and extra length of stay attributable to HAB and HCAB will be further evaluated using health economic models [50,51].

Although monitoring of nosocomial infection in developing countries is hampered by incomplete routine notification, our study has shown that careful evaluation of readily available routinely collected databases can provide valuable information on the incidence and trend of HAB and HCAB. The methodology used in our study could be applied to other geographical areas where microbiological facilities are available to provide a more comprehensive global picture of the importance of nosocomial infection as a cause of death.

Supporting Information

Figure S1 Location of participating hospitals. These were situated in: (1) Loei, (2) Udon Thani, (3) Nong Khai, (4) Nakhon Phanom, (5) Chaiyaphum, (6) Mahasarakarm, (7) Yasothorn, (8) Buriram, (9) Sisaket, and (10) Ubon Ratchathani.
(TIF)

Figure S2 Trend in hospital-acquired bacteremia (HAB) in ten provincial hospitals in Thailand.
(TIF)

Figure S3 Trend in healthcare-associated bacteremia (HCAB) in ten provincial hospitals in Thailand.
(TIF)

Table S1 List of participating hospitals.
(DOCX)

Acknowledgments

We gratefully acknowledge the Bacterial Infection in North East Thailand (BINET) network for providing microbiological and hospital admission data. BINET are comprised of Chalavit Limpavithayakula, Chatchawan Namsorn, Chadaporn Paungmala (Amnatchareon hospital), Chan Tantiwaraporn, Somsak Kitisriworapun, Kanyapak Panjaiya, Kridsada Sirichaisit (Buengkarn hospital), Chalit Thongprayoon, Somchai Jittai, Rattana Jirajaruporn (Buriram hospital), Sompong Charoenwat, Some Prasarn, Wiset Phosawang, Peeraphorn Lamworaphong (Chaiyaphum hospital), Pramoth Boonjian, Pattarawadee Wongmeema, Sunthorn Thongbai (Loei hospital), Sunthorn Yontrakul, Piyalak Siritaratiwat, Supanne Pisuttimarn (Mahasarakham hospital), Udom Pedphuwadee (Mukdaharn hospital), Somkid Suriyalert, Pichai Thongtaradol, Somsri Viriyaphun (Nakhon Phanom hospital), Kittisak Danwiboon, Kanjana Kehatan, Wannakorn Dechnorasing (Nongkhai hospital), Narong Uentrakul (Roi Ed hospital), Somsak Chaosirikul, Anek Jaddee, Soontorn Romaneeyapech (Sisaket hospital), Thongchai Triwiboonwanich, Saowarat Deekae, Vorathep Wuttisil (Surin hospital), Pramot Srisamang, Nittaya Teerawattanasook (Ubon Ratchathani hospital), Pichart Dolchalermyuttana, Yaowalau Loottrakul, Sayrung Sripavatakul (Udon Thani hospital), Charan Thongthap, Pongsathorn Siripoulsak, Chainakhon Kaewluang (Yasothorn hospital). We thank Mayura Malasit and Jintana Suwannapruk for their administrative support. We gratefully acknowledge the support provided by staff at the Mahidol-Oxford Tropical Medicine Research Unit and all participating hospitals. We thank Chutawat Luangsa-ard, Kraiwuth Sriporamanont, Mongkol Fungprasertkul and Dean Sherwood for computational support.

Author Contributions

Conceived and designed the experiments: MH PS MK AJ NPD SJP DL. Performed the experiments: MH MK AJ DL. Analyzed the data: MH AJ DL. Contributed to the writing of the manuscript: MH PS MK NL AJ NPD SJP BSC DL.

References

1. Allegranzi B, Bagheri Nejad S, Combescure C, Graafmans W, Attar H, et al. (2011) Burden of endemic health-care-associated infection in developing countries: systematic review and meta-analysis. Lancet 377(9761): p.228–41.
2. Vrijens F, Hulstaert F, Van de Sande S, Devriese S, Morales I, et al. (2010) Hospital-acquired, laboratory-confirmed bloodstream infections: linking national surveillance data to clinical and financial hospital data to estimate increased length of stay and healthcare costs. J Hosp Infect 75(3): p.158–62.
3. Wenzel RP, Edmond MB (2001) The impact of hospital-acquired bloodstream infections. Emerg Infect Dis 7(2): p.174–7.
4. Aiken AM, Mturi N, Njuguna P, Mohammed S, Berkley JA, et al. (2011) Risk and causes of paediatric hospital-acquired bacteraemia in Kilifi District Hospital, Kenya: a prospective cohort study. Lancet 378(9808): p.2021–7.
5. Askarian M, Mahmoudi H, Assadian O (2013) Incidence of Nosocomial Infections in a Big University Affiliated Hospital in Shiraz, Iran: A Six-month Experience. Int J Prev Med 4(3): p.366–72.
6. Kanoksil M, Jatapai A, Peacock SJ, Limmathurotsakul D (2013) Epidemiology, microbiology and mortality associated with community-acquired bacteremia in northeast Thailand: a multicenter surveillance study. PLoS One 8(1): p. e54714.
7. Opartkiattikul N, Bejrachandra S (2002) The external quality assessment schemes in Thailand. Rinsho Byori 50(2): p.121–5.
8. Shorr AF, Tabak YP, Killian AD, Gupta V, Liu LZ, et al. (2006) Healthcare-associated bloodstream infection: A distinct entity? Insights from a large U.S. database. Crit Care Med 34(10): p.2588–95.
9. Rodriguez-Bano J, Lopez-Prieto MD, Portillo MM, Retamar P, Natera C, et al. (2010) Epidemiology and clinical features of community-acquired, healthcare-associated and nosocomial bloodstream infections in tertiary-care and community hospitals. Clin Microbiol Infect 16(9): p.1408–13.
10. Hall KK, Lyman JA (2006) Updated review of blood culture contamination. Clin Microbiol Rev 19(4): p.788–802.
11. Wiersinga WJ, Currie BJ, Peacock SJ (2012) Melioidosis. N Engl J Med 367(11): p.1035–44.
12. Epidemiology BO (2011) Annual Epidemiology Surveillance Report 2010.
13. Fortin E, Rocher I, Frenette C, Tremblay C, Quach C (2012) Healthcare-associated bloodstream infections secondary to a urinary focus: the Quebec provincial surveillance results. Infect Control Hosp Epidemiol 33(5): p.456–62.
14. Lee MC, Saxinger L, Forgie SE, Taylor G (2010) Trends in nosocomial bloodstream infections following health care restructuring in Alberta between 1999 and 2005. Can J Infect Dis Med Microbiol 21(1): p. e1–5.
15. Mitt P, Adamson V, Loivukene K, Lang K, Telling K, et al. (2009) Epidemiology of nosocomial bloodstream infections in Estonia. J Hosp Infect 71(4): p.365–70.
16. Rosenthal VD, Bijie H, Maki DG, Mehta Y, Apisarnthanarak A, et al. (2012) International Nosocomial Infection Control Consortium (INICC) report, data summary of 36 countries, for 2004–2009. Am J Infect Control 40(5): p.396–407.
17. Peleg AY, Hooper DC (2010) Hospital-acquired infections due to gram-negative bacteria. N Engl J Med 362(19): p.1804–13.
18. Pereira CA, Marra AR, Camargo LF, Pignatari AC, Sukiennik T, et al. (2013) Nosocomial bloodstream infections in Brazilian pediatric patients: microbiology, epidemiology, and clinical features. PLoS One 8(7): p. e68144.
19. Johnson AP (2011) Methicillin-resistant Staphylococcus aureus: the European landscape. J Antimicrob Chemother 66 Suppl 4: p. iv43–iv48.
20. Son JS, Song JH, Ko KS, Yeom JS, Ki HK, et al. (2010) Bloodstream infections and clinical significance of healthcare-associated bacteremia: a multicenter surveillance study in Korean hospitals. J Korean Med Sci 25(7): p.992–8.
21. Rosenthal VD, Maki DG, Rodrigues C, Alvarez-Moreno C, Leblebicioglu H, et al. (2010) Impact of International Nosocomial Infection Control Consortium (INICC) strategy on central line-associated bloodstream infection rates in the intensive care units of 15 developing countries. Infect Control Hosp Epidemiol 31(12): p.1264–72.
22. Rosenthal VD, Ramachandran B, Villamil-Gomez W, Armas-Ruiz A, Navoa-Ng JA, et al. (2012) Impact of a multidimensional infection control strategy on central line-associated bloodstream infection rates in pediatric intensive care units of five developing countries: findings of the International Nosocomial Infection Control Consortium (INICC). Infection 40(4): p.415–23.
23. Rosenthal VD, Duenas L, Sobreyra-Oropeza M, Ammar K, Navoa-Ng JA, et al. (2013) Findings of the International Nosocomial Infection Control Consortium (INICC), part III: effectiveness of a multidimensional infection control approach to reduce central line-associated bloodstream infections in the neonatal intensive care units of 4 developing countries. Infect Control Hosp Epidemiol 34(3): p.229–37.
24. Jaggi N, Rodrigues C, Rosenthal VD, Todi SK, Shah S, et al. (2013) Impact of an international nosocomial infection control consortium multidimensional approach on central line-associated bloodstream infection rates in adult intensive care units in eight cities in India. Int J Infect Dis 17(12): p. e1218–24.
25. Leblebicioglu H, Ozturk R, Rosenthal VD, Akan OA, Sirmatel F, et al. (2013) Impact of a multidimensional infection control approach on central line-associated bloodstream infections rates in adult intensive care units of 8 cities of Turkey: findings of the International Nosocomial Infection Control Consortium (INICC). Ann Clin Microbiol Antimicrob 12: p.10.
26. Higuera F, Rosenthal VD, Duarte P, Ruiz J, Franco G, et al. (2005) The effect of process control on the incidence of central venous catheter-associated bloodstream infections and mortality in intensive care units in Mexico. Crit Care Med 33(9): p.2022–7.
27. Rosenthal VD, Guzman S, Pezzotto SM, Crnich CJ (2003) Effect of an infection control program using education and performance feedback on rates of intravascular device-associated bloodstream infections in intensive care units in Argentina. Am J Infect Control 31(7): p.405–9.
28. Klevens RM, Edwards JR, Richards CL Jr, Horan TC, Gaynes RP, et al. (2007) Estimating health care-associated infections and deaths in U.S. hospitals, 2002. Public Health Rep 122(2): p.160–6.
29. Cheng AC, West TE, Limmathurotsakul D, Peacock SJ (2008) Strategies to reduce mortality from bacterial sepsis in adults in developing countries. PLoS Med 5(8): p. e175.
30. Duenas L, Bran de Casares A, Rosenthal VD, Jesus Machuca L (2011) Device-associated infections rates in pediatrics and neonatal intensive care units in El Salvador: findings of the INICC. J Infect Dev Ctries 5(6): p.445–51.
31. Guanche-Garcell H, Requejo-Pino O, Rosenthal VD, Morales-Perez C, Delgado-Gonzalez O, et al. (2011) Device-associated infection rates in adult intensive care units of Cuban university hospitals: International Nosocomial Infection Control Consortium (INICC) findings. Int J Infect Dis 15(5): p. e357–62.
32. Hu B, Tao L, Rosenthal VD, Liu K, Yun Y, et al. (2013) Device-associated infection rates, device use, length of stay, and mortality in intensive care units of 4 Chinese hospitals: International Nosocomial Control Consortium findings. Am J Infect Control 41(4): p.301–6.
33. Kubler A, Duszynska W, Rosenthal VD, Fleischer M, Kaiser T, et al. (2012) Device-associated infection rates and extra length of stay in an intensive care unit of a university hospital in Wroclaw, Poland: International Nosocomial Infection Control Consortium's (INICC) findings. J Crit Care 27(1): p.105 e5–10.
34. Navoa-Ng JA, Berba R, Galapia YA, Rosenthal VD, Villanueva VD, et al. (2011) Device-associated infections rates in adult, pediatric, and neonatal

intensive care units of hospitals in the Philippines: International Nosocomial Infection Control Consortium (INICC) findings. Am J Infect Control 39(7): p.548–54.
35. Rasslan O, Seliem ZS, Ghazi IA, El Sabour MA, El Kholy AA, et al. (2012) Device-associated infection rates in adult and pediatric intensive care units of hospitals in Egypt. International Nosocomial Infection Control Consortium (INICC) findings. J Infect Public Health 5(6): p.394–402.
36. Tao L, Hu B, Rosenthal VD, Gao X, He L (2011) Device-associated infection rates in 398 intensive care units in Shanghai, China: International Nosocomial Infection Control Consortium (INICC) findings. Int J Infect Dis 15(11): p. e774–80.
37. Rosenthal VD, Guzman S, Orellano PW (2003) Nosocomial infections in medical-surgical intensive care units in Argentina: attributable mortality and length of stay. Am J Infect Control 31(5): p.291–5.
38. Rosenthal VD, Guzman S, Crnich C (2004) Device-associated nosocomial infection rates in intensive care units of Argentina. Infect Control Hosp Epidemiol 25(3): p.251–5.
39. Moreno CA, Rosenthal VD, Olarte N, Gomez WV, Sussmann O, et al. (2006) Device-associated infection rate and mortality in intensive care units of 9 Colombian hospitals: findings of the International Nosocomial Infection Control Consortium. Infect Control Hosp Epidemiol 27(4): p.349–56.
40. Ramirez Barba EJ, Rosenthal VD, Higuera F, Oropeza MS, Hernandez HT, et al. (2006) Device-associated nosocomial infection rates in intensive care units in four Mexican public hospitals. Am J Infect Control 34(4): p.244–7.
41. Rosenthal VD, Maki DG, Salomao R, Moreno CA, Mehta Y, et al. (2006) Device-associated nosocomial infections in 55 intensive care units of 8 developing countries. Ann Intern Med, 2006. 145(8): p.582–91.
42. Leblebicioglu H, Rosenthal VD, Arikan OA, Ozgultekin A, Yalcin AN, et al. (2007) Device-associated hospital-acquired infection rates in Turkish intensive care units. Findings of the International Nosocomial Infection Control Consortium (INICC). J Hosp Infect 65(3): p.251–7.
43. Mehta A, Rosenthal VD, Mehta Y, Chakravarthy M, Todi SK, et al. (2007) Device-associated nosocomial infection rates in intensive care units of seven Indian cities. Findings of the International Nosocomial Infection Control Consortium (INICC). J Hosp Infect 67(2): p.168–74.
44. Cuellar LE, Fernandez-Maldonado E, Rosenthal VD, Castaneda-Sabogal A, Rosales R, et al. (2008) Device-associated infection rates and mortality in intensive care units of Peruvian hospitals: findings of the International Nosocomial Infection Control Consortium. Rev Panam Salud Publica 24(1): p.16–24.
45. Rosenthal VD (2008) Device-associated nosocomial infections in limited-resources countries: findings of the International Nosocomial Infection Control Consortium (INICC). Am J Infect Control 36(10): p. S171 e7–12.
46. Salomao R, Rosenthal VD, Grimberg G, Nouer S, Blecher S, et al. (2008) Device-associated infection rates in intensive care units of Brazilian hospitals: findings of the International Nosocomial Infection Control Consortium. Rev Panam Salud Publica 24(3): p.195–202.
47. Madani N, Rosenthal VD, Dendane T, Abidi K, Zeggwagh AA, et al. (2009) Health-care associated infections rates, length of stay, and bacterial resistance in an intensive care unit of Morocco: findings of the International Nosocomial Infection Control Consortium (INICC). Int Arch Med 2(1): p.29.
48. Friedman C, Richter D, Skylis T, Brown D (1984) Process surveillance: auditing infection control policies and procedures. Am J Infect Control 12(4): p.228–32.
49. Baker OG (1997) Process surveillance: an epidemiologic challenge for all health care organizations. Am J Infect Control 25(2): p.96–101.
50. Higuera F, Rangel-Frausto MS, Rosenthal VD, Soto JM, Castanon J, et al. (2007) Attributable cost and length of stay for patients with central venous catheter-associated bloodstream infection in Mexico City intensive care units: a prospective, matched analysis. Infect Control Hosp Epidemiol 28(1): p.31–5.
51. Rosenthal VD, Guzman S, Migone O, Crnich CJ (2003) The attributable cost, length of hospital stay, and mortality of central line-associated bloodstream infection in intensive care departments in Argentina: A prospective, matched analysis. Am J Infect Control 31(8): p.475–80.

Comparative efficacy of interventions to promote hand hygiene in hospital: systematic review and network meta-analysis

Nantasit Luangasanatip,[1,2] Maliwan Hongsuwan,[1] Direk Limmathurotsakul,[1,3] Yoel Lubell,[1,4] Andie S Lee,[5,6] Stephan Harbarth,[5] Nicholas P J Day,[1,4] Nicholas Graves,[2,7] Ben S Cooper[1,4]

[1]Mahidol-Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand
[2]School of Public Health, Queensland University of Technology, Brisbane, Australia
[3]Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand
[4]Centre for Tropical Medicine and Global Health, Nuffield Department of Clinical Medicine, University of Oxford, Oxford, UK
[5]Infection Control Program, University of Geneva Hospitals and Faculty of Medicine, Geneva 1211, Switzerland
[6]Departments of Infectious Diseases and Microbiology, Royal Prince Alfred Hospital, Sydney 2050, Australia
[7]Institute of Health and Biomedical Innovation, Queensland University of Technology, Brisbane, Australia

Correspondence to: N Luangasanatip, Mahidol-Oxford Tropical Medicine Research Unit, 420/6 60th Anniversary Chalermprakiat Building; 3rd Floor, Rajvithi Road, Bangkok Thailand 10400
nantasit@tropmedres.ac

Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/bmj.h3728)

Cite this as: *BMJ* 2015;351:h3728
doi: 10.1136/bmj.h3728

Accepted: 22 June 2015

ABSTRACT

OBJECTIVE
To evaluate the relative efficacy of the World Health Organization 2005 campaign (WHO-5) and other interventions to promote hand hygiene among healthcare workers in hospital settings and to summarize associated information on use of resources.

DESIGN
Systematic review and network meta-analysis.

DATA SOURCES
Medline, Embase, CINAHL, NHS Economic Evaluation Database, NHS Centre for Reviews and Dissemination, Cochrane Library, and the EPOC register (December 2009 to February 2014); studies selected by the same search terms in previous systematic reviews (1980-2009).

REVIEW METHODS
Included studies were randomised controlled trials, non-randomised trials, controlled before-after trials, and interrupted time series studies implementing an intervention to improve compliance with hand hygiene among healthcare workers in hospital settings and measuring compliance or appropriate proxies that met predefined quality inclusion criteria. When studies had not used appropriate analytical methods, primary data were re-analysed. Random effects and network meta-analyses were performed on studies reporting directly observed compliance with hand hygiene when they were considered sufficiently homogeneous with regard to interventions and participants. Information on resources required for interventions was extracted and graded into three levels.

RESULTS
Of 3639 studies retrieved, 41 met the inclusion criteria (six randomised controlled trials, 32 interrupted time series, one non-randomised trial, and two controlled before-after studies). Meta-analysis of two randomised controlled trials showed the addition of goal setting to WHO-5 was associated with improved compliance (pooled odds ratio 1.35, 95% confidence interval 1.04 to 1.76; I^2=81%). Of 22 pairwise comparisons from interrupted time series, 18 showed stepwise increases in compliance with hand hygiene, and all but four showed a trend for increasing compliance after the intervention. Network meta-analysis indicated considerable uncertainty in the relative effectiveness of interventions, but nonetheless provided evidence that WHO-5 is effective and that compliance can be further improved by adding interventions including goal setting, reward incentives, and accountability. Nineteen studies reported clinical outcomes; data from these were consistent with clinically important reductions in rates of infection resulting from improved hand hygiene for some but not all important hospital pathogens. Reported costs of interventions ranged from \$225 to \$4669 (£146-£3035; €204-€4229) per 1000 bed days.

CONCLUSION
Promotion of hand hygiene with WHO-5 is effective at increasing compliance in healthcare workers. Addition of goal setting, reward incentives, and accountability strategies can lead to further improvements. Reporting of resources required for such interventions remains inadequate.

WHAT IS ALREADY KNOWN ON THIS TOPIC
Hand hygiene among healthcare workers is possibly one of the most effective measures to reduce healthcare associated infections, but compliance remains poor in many hospital settings

In 2005 WHO launched a campaign to improve hand hygiene in healthcare settings by promoting a multimodal strategy consisting of five components: system change, training and education, observation and feedback, reminders in the hospital, and a hospital safety climate

WHAT THIS STUDY ADDS
These meta-analyses provide evidence that the WHO campaign is effective at increasing compliance with hand hygiene in healthcare workers

There is evidence that additional interventions (used in conjunction with the WHO campaign elements), including goal setting, reward incentive, and accountability, can lead to further improvements

Reporting on resource implications of such interventions is limited

Introduction
At any point in time more than 1.4 million patients around the world experience healthcare associated infections.[1,2] Such infections cause excess morbidity and are associated with increased mortality.[2,3] Direct contact between patients and healthcare workers who are transiently contaminated with nosocomial pathogens is believed to be the primary route of transmission for several organisms and can lead to patients becoming colonised or infected. Although hand hygiene is widely thought to be the most important activity for the prevention of nosocomial infections, a review of hand hygiene studies by the World Health Organization (WHO) found that baseline compliance with hand hygiene among healthcare workers was on average only 38.7% (range 5-89%).[4]

In 2005, the WHO World Alliance for Patient Safety launched a campaign, the First Global Patient Safety Challenge—"Clean Care is Safer Care"—aiming to improve hand hygiene in healthcare.[4] This campaign

(WHO-5) promotes a multimodal strategy consisting of five components: system change, training and education, observation and feedback, reminders in the hospital, and a hospital safety climate. More recently, additional strategies for improving hand hygiene have been evaluated, including those based on behavioural theory.

We assessed the relative effectiveness of WHO-5 and other strategies for improving compliance with hand hygiene in healthcare workers in hospital settings. Evaluation of the evidence for the effectiveness of different interventions is complicated by three factors: firstly, most evaluations of interventions to promote hand hygiene use non-randomised study designs, and in many cases the reported analysis is inappropriate or methodological quality is too low to allow meaningful conclusions to be drawn;[5-8] secondly, there is wide variation between studies in the activities to promote hand hygiene used in the comparison group; thirdly, direct head-to-head comparisons of most interventions are lacking.[7]

We aimed to overcome these problems by restricting attention to randomised trials and high quality non-randomised studies, re-analysing data when necessary; explicitly accounting for activities to promote hand hygiene in the comparison group in each study; and using network meta-analysis to allow indirect comparison between interventions.

We also summarise information on changes in clinical and microbiological outcomes associated with interventions when this was reported. Information on resources used in different interventions is essential for those wanting to implement such interventions or evaluate their cost effectiveness.[9 10] An additional aim was therefore to document information on resources used in interventions to promote hand hygiene.

Methods

We developed a protocol and used systematic methods to identify relevant studies, screen study eligibility, and assess study quality. This protocol was not registered. This review is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[11]

Search strategy

We used a two stage search strategy. Firstly, we obtained all studies considered in two previous reviews (covering the period up to November 2009), including those that had been reported as failing to meet inclusion criteria.[5 6] Secondly, we extended the search from these studies from December 2009 to February 2014. We searched Medline, Embase, Cumulative Index to Nursing and Allied Health (CINAHL), Database of Abstracts of Reviews of Effects (DARE), National Health Service Economic Evaluation Database (NHS-EED), National Health Service Centre for Reviews and Dissemination (NHS-CRD) and British Nursing Index (BNI), Cochrane Library (Cochrane database of systematic reviews, Cochrane central register of controlled trials, Cochrane methodology register, Health Technology assessment database), Clinical Trial.gov, Current Clinical Control trial, Cochrane Effective Practice and Organisation of Care Group (EPOC) register, American College of Physicians journal, and reviews of evidence based medicine. Results were limited to peer reviewed publications. To validate previous search results we also repeated the electronic search for three earlier years (1980, 1995, and 2009). The complete search strategy is provided in appendix 1.

Inclusion and exclusion

Studies were included if they met all the following initial criteria: they evaluated one or more interventions intended to improve hand hygiene compliance among healthcare workers in a hospital setting; they measured compliance with hand hygiene using opportunities with prespecified indications or using proxies linked to compliance (such as consumption of soap and alcohol hand rub); they were either randomised controlled trials, non-randomised trials, controlled before-after studies, or used an interrupted time series design.

We placed no restrictions on promotion of hand hygiene in the comparison group. Studies were excluded if they were not reported in peer reviewed publications or not written in English.

We applied a methodological filter by excluding studies that failed meet minimal quality criteria specified by the Cochrane Effectiveness Practice and Organisation of Care Group (EPOC). Acceptable study designs were randomised controlled trials and non-randomised trials (with at least two intervention and two control sites); controlled before-after studies (with outcome measures before and after the intervention from at least two intervention and two comparable control sites); and interrupted time series (with a clearly defined point in time for the intervention and outcome measures from at least three time points in both baseline and intervention periods).[12 13]

Patient involvement

No patients were involved in setting the research question or the outcome measures, nor were they involved in the design and implementation of the study. There are no plans to involve patients in dissemination.

Data extraction and assessment of quality

Two reviewers (NL and BSC) independently screened the titles and abstracts of the citations obtained from the search to assess the eligibility. Consensus was reached by discussion if initial assessments differed. NL evaluated the full text and abstracted data, which was checked by BSC.

The reviewers abstracted data including study design and duration, population, activities to promote hand hygiene in both intervention and comparison groups, hand hygiene outcomes, clinical and microbiological outcomes, measurement methods, and settings. When possible, we classified hand hygiene promotion activities according to WHO guidelines on hand hygiene in healthcare.[4] We grouped activities into eight components: system change, education, feedback, reminders,

Table 1 | Description of eight components of interventions to promote hand hygiene in healthcare workers

Component	Description
System change*	Ensuring necessary infrastructure is available including access to water, soap and towels and alcohol based handrub at point of care
Education and training	Providing training or educational programme on importance of hand hygiene and correct procedures for hand hygiene for healthcare workers
Feedback	Monitoring hand hygiene practices among healthcare workers while providing compliance feedback to staff
Reminders at workplace	Prompting healthcare workers either through printed material, verbal reminders, electronic communications or other methods, to remind them about importance of hand hygiene and appropriate indications and procedures
Institutional safety climate	Active participation at institutional level, creating environment allowing prioritisation of hand hygiene
Goal setting	Setting of specific goals aimed at improving compliance with hand hygiene, which can both apply at individual and group level and can include healthcare associated infection rates
Reward incentives	Interventions providing any reward incentive for participants completing a particular task or reaching a certain level of compliance. Both non-financial and financial rewards are included
Accountability	Interventions involved with improving healthcare workers' accountability both at individual and unit level

*If the intervention period included changing the location or formulation of alcohol based handrub or installing more handrub dispensers, the baseline intervention was counted as no intervention or standard practice (no system change component), even if alcohol based handrub had been used during the baseline period.

safety climate, incentives, goal setting, and accountability (table 1). Results and raw compliance data from each study were extracted for further re-analyses. In addition, we extracted the costs of hand hygiene interventions or data on use of resources (materials and time spent on interventions) when appropriate. Additional information was obtained from the authors if it was not clear from the manuscript. For all included studies we used prespecified definitions to record the level of information (high, moderate, or low) about resources used for promotion of hand hygiene (see appendix 2).

Assessment of risk of bias in included studies

We used the Cochrane Collaboration's tool to assess risk of bias.[14] Nine standard criteria for randomised controlled trials, non-randomised trials, and controlled before-after studies and seven standard criteria for interrupted time series were applied and used to classify each study's risk of bias as low, high, or unclear.

Data synthesis and statistical analysis

Data synthesis was performed separately for different study designs. The primary evidence synthesis was based on studies that used direct observation to measure compliance with hand hygiene. We restricted our analysis to this outcome because it reflects the opportunities for hand hygiene.

For randomised controlled trials, we used Cochrane Review Manager (RevMan; version 5.1) to calculate the natural logarithm of the odds ratio and associated variance to estimate the pooled odds ratio with a random effects model.[15] The same method was applied to non-randomised trials, and controlled before-after studies if applicable. Heterogeneity between studies was assessed with the I^2 statistic. Risk of publication bias was evaluated with an enhanced contour funnel plot.[16 17]

For interrupted time series, if re-analysis was required, we used a generalised linear segmented regression analysis to estimate the stepwise change in level and change in trend associated with the intervention.[18] This approach is similar to that proposed by Ramsey and colleagues[19] and Vidanapathirana and colleagues,[20] except that it accounts for the binomial nature of the data, appropriately weighting each data point by the number of observations. We accounted for any evidence of autocorrelation by using Newey-West standard errors.[21] Analysis was performed with Stata 13 (Statacorp LP, College Station, TX). We then estimated two summary measures that combined both stepwise and trend changes. Firstly, we calculated the mean natural logarithm of the odds ratio for hand hygiene associated with the intervention, a measure of relative improvement. Secondly, we calculated the mean percentage change in compliance in the period after the intervention (compared with that expected if there had been no intervention), an absolute measure of improvement in compliance. Standard errors were derived with the delta method by using the emdbook package in R.[22 23] Appendix 3 provides full details.

Network meta-analysis

Network meta-analysis aims to combine all of the evidence, both direct and indirect, to estimate the comparative efficacy of all the interventions.[24] Each intervention strategy is represented by a node in the network. If a study directly compares two interventions they are directly connected by a link on the network and a direct comparison is possible. If two interventions are connected indirectly (for example, if there are studies comparing each with a third intervention), then indirect comparison is possible.

We used network meta-analysis to compare the relative effectiveness of four different strategies: no promotion of hand hygiene, single component interventions, WHO-5, and WHO-5 and others (table 2). We included in the network meta-analysis those studies that included only these strategies and permitted a segmented regression analysis and directly observed compliance with hand hygiene.[25 26]

The effect sizes obtained from each comparison were combined in a network meta-analysis with a random effects model.[25] Effect sizes were taken as the mean of the natural logarithm of the odds ratio for the hand hygiene intervention as estimated with the segmented regression model. Intervention rankings and associated credible intervals were obtained. Model fitting for the meta-analysis was carried out within a Bayesian

Table 2 | Mean odds ratios with 95% credible intervals for interventions strategies to promote hand hygiene. Results are from random effects network meta-analysis model

Strategies*	Description	Mean OR (95% credible interval)
None/current practice	No intervention or current practice	Reference
Single intervention	Single intervention (system change or education)	4.30 (0.43 to 46.57)
WHO-5†	WHO-5 components	6.51 (1.58 to 31.91)
WHO-5* + others	WHO-5 plus incentives, goal setting, or accountability	11.83 (2.67 to 53.79)

*Model fit statistic: posterior mean residual deviance=10.40 and deviance information criterion (DIC)=23.86.
†Contained five components: system change, education, feedback, reminders, and institutional safety climate (see table 1 for details).

framework using WinBUGS.[26] Inconsistency checks were performed for closed loops in the network.[27] Full model details are provided in appendix 4.

We performed a sensitivity analysis by excluding studies that implemented multicomponent strategies in a stepwise manner without sufficient data to evaluate individual components. This led to the exclusion of three studies.[28-30]

Results

Overall description

Figure 1 shows a summary of the review process. Of 3639 studies screened, 142 studies met initial inclusion criteria and 41 of these met EPOC criteria. Among these 41 studies, six were randomised controlled trials (including three cluster randomised controlled trials),[31-36] 32 were interrupted time series,[28-30 37-65] one was a non-randomised trial,[66] and two were controlled before-after studies.[67 68] Appendix 5 give details of the reasons for exclusion. Applying our search strategy to three years covered by previous reviews did not yield any studies meeting our inclusion criteria that had not already been included.

Seventeen studies applied interventions to the whole hospital, while 21 studies enrolled hospital wards. Three studies allocated interventions to specific healthcare workers.[31 33 36] Twenty five studies were conducted in either a hospital-wide setting or combined intensive care units and general wards, while 11 were conducted in intensive care units or general wards alone. Of 10 studies conducted in more than one hospital, three included two or more countries.[42 48 50] Only five of the 41 studies were conducted in low or middle income countries.[33 36 46 50 51]

Study periods ranged from two months to six years. In 11 studies the period was up to one year; in 17 studies it was more than a year and up to three years; and in 13 it was more than three years. Among the 32 interrupted time series, only 11 were longer than 12 months.

In 34 studies hand hygiene was observed in all types of healthcare workers with patient contact, while six studies considered only nurses and/or nursing assistants.[33 34 36 60 64 68] One study recruited only nursing students as participants.[54] One study also included patients' relatives.[39]

Six studies used a single faceted intervention: four implemented education alone[33 46 54 68] and two applied system change or reminders.[39 44] Seventeen studies used interventions equivalent to WHO-5, and six of these added supplemental interventions including goal setting, incentives, and accountability.[28 34 40 45 56 66] Nineteen studies implemented interventions with two to four components; four of these applied components not in WHO-5, including goal setting and incentives.[37 38 41 59]

Thirty studies (four randomised controlled trials, 25 interrupted time series, and one non-randomised trial) used direct observation to measure compliance with hand hygiene. Two of these used a combination of video recorders and external observers.[37 38] Proxy measures were assessed in 19 studies including the rate of hand hygiene events, consumption of hand hygiene products (alcohol hand rub or soap), and a hand hygiene score checklist (two randomised controlled trials, 15 interrupted time series, and two controlled before and after studies). Clinical outcomes were reported in 19 studies.[28-30 35 42 46-52 55-57 59 62 63 66 67 69] Appendix 6 provides full study characteristics including study design, setting, intervention, and comparison groups.

Examination of funnel plots (appendix 7) did not provide any clear evidence of publication bias, though evidence for or against such bias was limited by the fact that there were no more than four studies for any pairwise comparison of strategies.

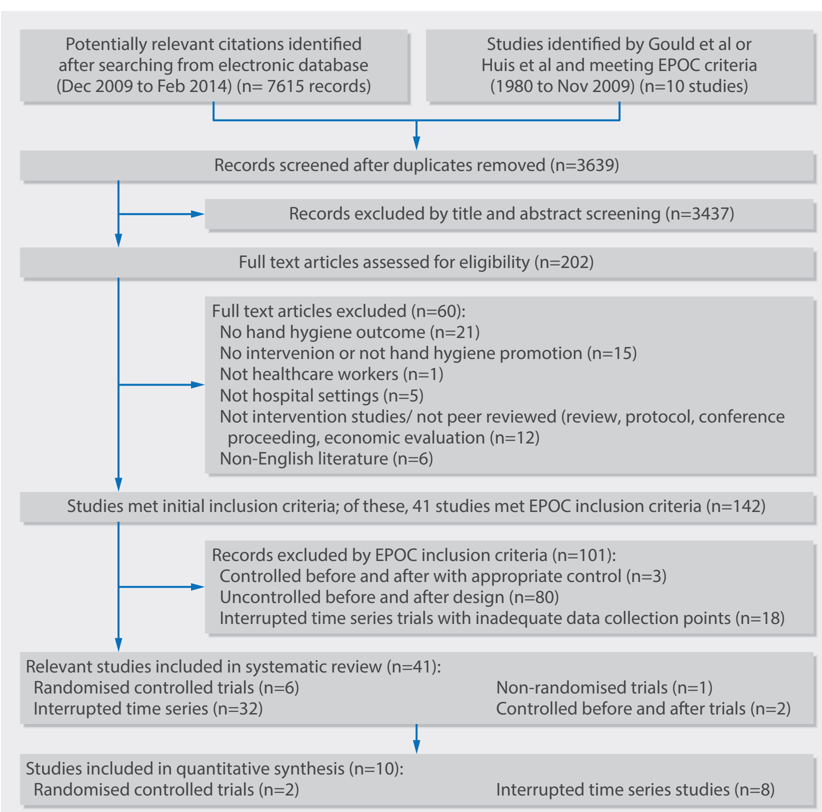


Fig 1 | Flow chart of study identification in systematic review of interventions to promote hand hygiene in healthcare workers

Quality assessment

Ten studies were considered to have a high risk of bias. Thirty one had either low or unclear risk. High risk of bias was present in all three non-randomised trials or controlled before-after studies but only in seven out of

32 interrupted time series. No randomised controlled trials or cluster randomised controlled trials were thought to have a high risk of bias (fig 2).

The two controlled before-after studies[67 68] had high risks for inadequate allocation sequence and concealment, while one non-randomised trial[66] had high risk of dissimilarity in baseline outcome between experimental and control groups.

Fourteen studies (34%) had a low risk of bias due to the knowledge of allocated intervention, as these studies either measured objective outcomes (such as alcohol consumption or output from electronic counting devices) or stated that the observers were blinded to the intervention. The rest of the studies had unclear risk as they did not report whether the observers were blinded.

Risk of selective outcome reporting was unclear in 33 studies as pre-specified protocols were reported only in three randomised controlled trials.[32 34 35] Two of the interrupted time series had a high risk of selective outcome reporting as they reported on a non-periodical basis.[28 59] Among the interrupted time series, six had a high risk that outcomes were affected by other interventions such as a universal chlorhexidine body washing programme,[42 63] reinforcement of standard precautions,[42] screening and decolonisation for multidrug-resistant micro-organisms,[48] quality improvement program,[46 59] and antibiotic use and healthcare associated infections control policy implemented at the same time.[56]

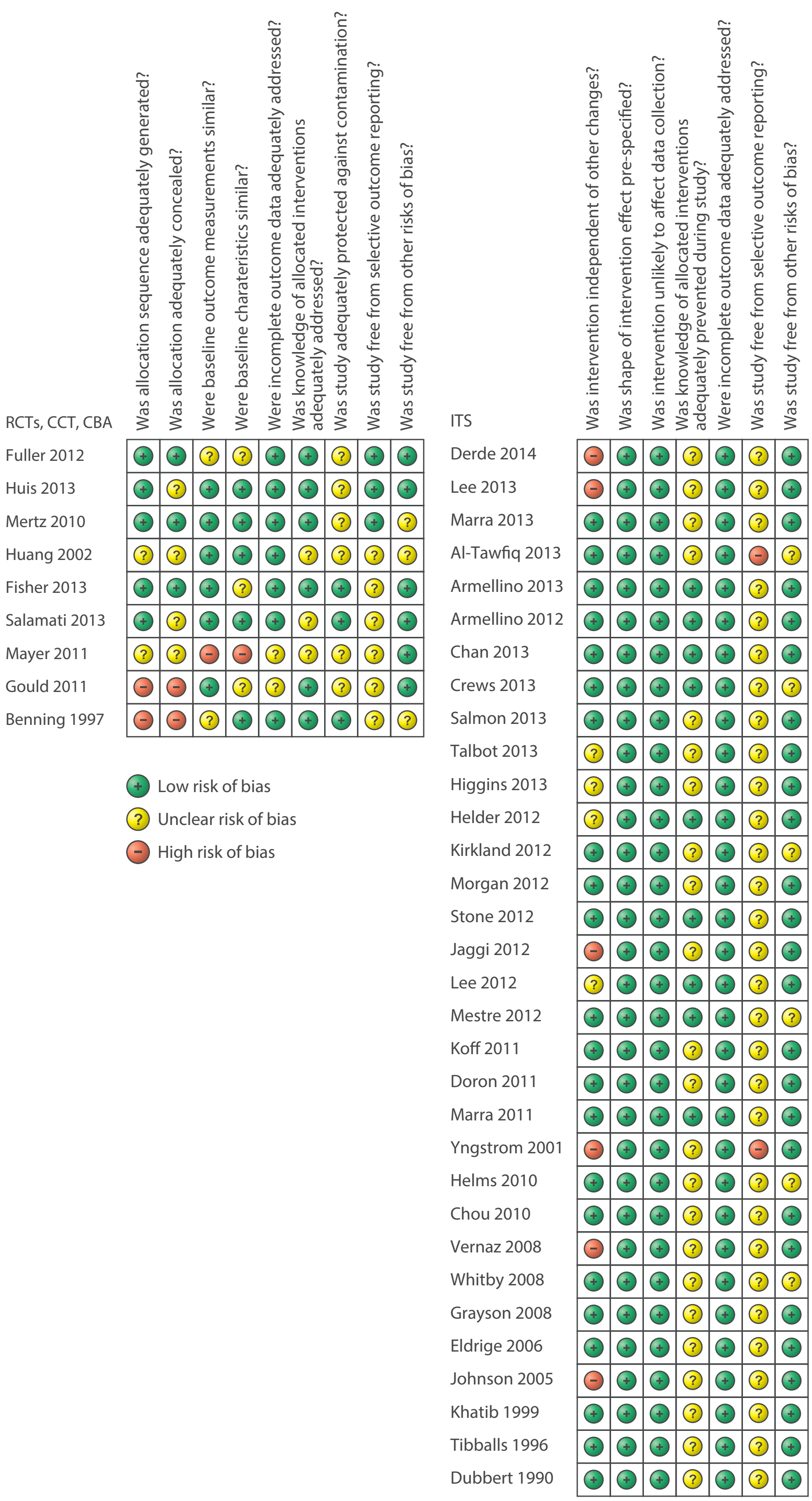


Fig 2 | **Assessment of risk of bias in included studies of interventions to promote hand hygiene in healthcare workers**

Meta-analysis/data synthesis

Randomised controlled trials

Four of six randomised controlled trials measured compliance with hand hygiene by direct observation with indications similar to WHO-5.[32-35] Two of these studies compared WHO-5 with WHO-5 combined with goal setting (WHO-5+).[32 34] Huis and colleagues performed a cluster randomised trial in 67 wards from three hospitals in the Netherlands.[34] Compliance immediately after the intervention increased from 23% to 42% in the WHO-5 arm and from 20% to 53% in the WHO-5+ arm; in both arms improvements were sustained six months later. Fuller and colleagues used a three year stepped wedge design in 16 intensive care units and 44 acute care of the elderly wards and reported an absolute increase in compliance of 13-18% and 10-13%, respectively, in implementing wards.[32] Only 33 of 60 enrolled wards, however, implemented the intervention (22 out of 44 elderly wards and 11 out of 16 intensive care units), and the intention to treat analysis did not show increased compliance in the elderly wards while compliance in intensive care units increased by 7-9%. Meta-analysis (with intention to treat results) provided evidence favouring the WHO-5+ strategy. The pooled odds ratio was 1.35 (95% confidence interval 1.04 to 1.76; I^2=81%) (fig 3). The large heterogeneity seemed to be caused by the low fidelity to intervention in acute care of the elderly wards. Per protocol analyses gave similar odds ratios for compliance to the study by Huis and colleagues (1.67 (95% confidence interval 1.28 to 2.22) for elderly wards and 2.09 (1.55 to 2.81) for intensive care units). Two other randomised controlled trials directly reported observed compliance with hand hygiene. An individually randomised trial of an education programme versus no intervention for nurses in China reported an absolute improvement in compliance of

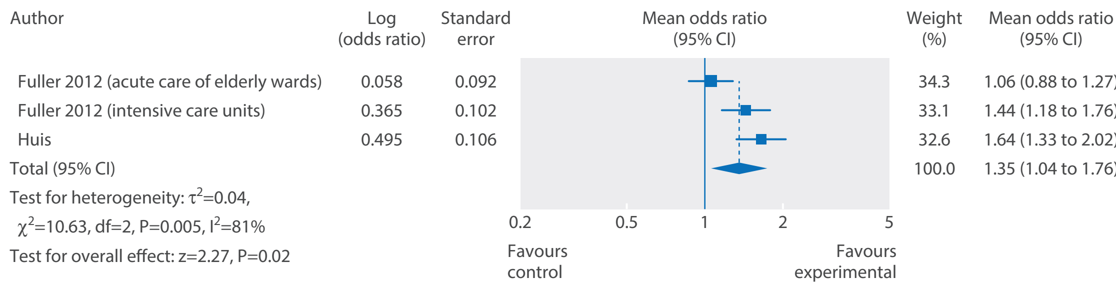


Fig 3 | Forest plot of the associations between WHO-5 and goal setting compared with WHO-5 alone and compliance with hand hygiene from randomised controlled trials using intention to treat results

32.7% (95% confidence interval 15.6% to 49.7%) for opportunities before contact with patients and 20.4% (5.6% to 35.2%) for opportunities after contact (baseline compliance before and after contact was about 25% and 37%, respectively, in both arms).[33] In Canada, a cluster randomised trial of a bundle of education, performance feedback, and visual reminders in 30 hospital units where alcohol hand rub was available at point of care in both arms (but with no other interventions in the control arm) reported a higher adherence after the intervention in the intervention arm (mean difference 6.3%, 95% confidence interval 4.3% to 8.4%).[35] In both arms baseline compliance was low (16%).

Fisher and colleagues randomised individuals to either a control group where hand hygiene was not actively promoted or an intervention arm that used audio reminders and individual feedback.[31] They assessed compliance using an automated system at entry to and exit from patients' rooms. The intervention was associated with a 6.8% (95% confidence interval 2.5% to 11.1%) improvement in compliance. Salamati and colleagues randomised nursing personnel to either a motivational interviewing intervention (a behaviour modification approach initially developed to treat patients with alcoholism) or a control group.[36] Both arms also received an educational intervention. The outcome measure was a composite hand hygiene score, which was found to increase in the intervention arm. The scoring details, however, were unclear.

Interrupted time series

Of 32 interrupted time series, 25 measured hand hygiene compliance. Only 18 studies with direct observation, however, reported the number of observations at each time point, making them eligible for re-analysis.[28-30,37,38,40-46,48,50,54,56,60,64,65] As some of these studies were conducted at multiple sites[48] or had multiple intervention phases,[56] 22 pairwise comparisons from these 18 studies were available for re-analysis (fig 4). In four studies there was evidence of positive first order autocorrelation.[37,38,40,56]

The baseline compliance ranged from 7.6% to 91.3%. Twelve of 22 comparisons showed a declining trend in compliance during the period before intervention; seven of these did not report any activities to promote hand hygiene before intervention, while another four used only education or reminders. Fifteen pairwise contrasts showed a positive change in trend for compliance with hand hygiene after the intervention (table 3). All but four contrasts showed both stepwise increases in compliance with hand hygiene associated with the intervention and increases in mean compliance in the period after intervention compared with that expected in the absence of the intervention. The range was wide: the mean change in hand hygiene attributed to the intervention varied between a decrease of 14.8% and an increase of 83.3% (table 3). Two studies had an intervention period lasting at least two years; neither showed evidence for any decline in compliance over this period.[40,41] In only one study was there a net trend for decreasing compliance after the intervention (fig 4).[45]

Non-randomised trials and controlled before-after studies

Mayer and colleagues compared WHO-5 and reward incentives (WHO-5+) with a combination of system change, education, and feedback using a staggered introduction of an intervention bundle, across four out of six patient units.[66] The WHO-5+ intervention was associated with improved compliance, which increased from 40% to 64% in one two-unit cohort and from 34% to 49% in the other.

Benning and colleagues reported a hospital-wide trend of increased soap and alcohol consumption in both intervention (package of system change, reminders, and safety climate) and control (no intervention) groups but found no evidence of an increased effect in the intervention group.[67] Gould and colleagues found no evidence of improvement in frequency of hand decontamination in surgical intensive care wards resulting from a series of educational lectures compared with no intervention (control).[68]

Analysis of interrupted time series and network meta-analysis

Among the 22 pairwise comparisons from interrupted time series, 18 had clear details about interventions and similar indications for compliance with hand hygiene among qualified healthcare workers. In 16 of these the intervention period included additional intervention components alongside measures to promote hand hygiene used in the baseline period, and all outcome data favoured the intervention (fig 5). In the two comparisons where there was no improvement in hand

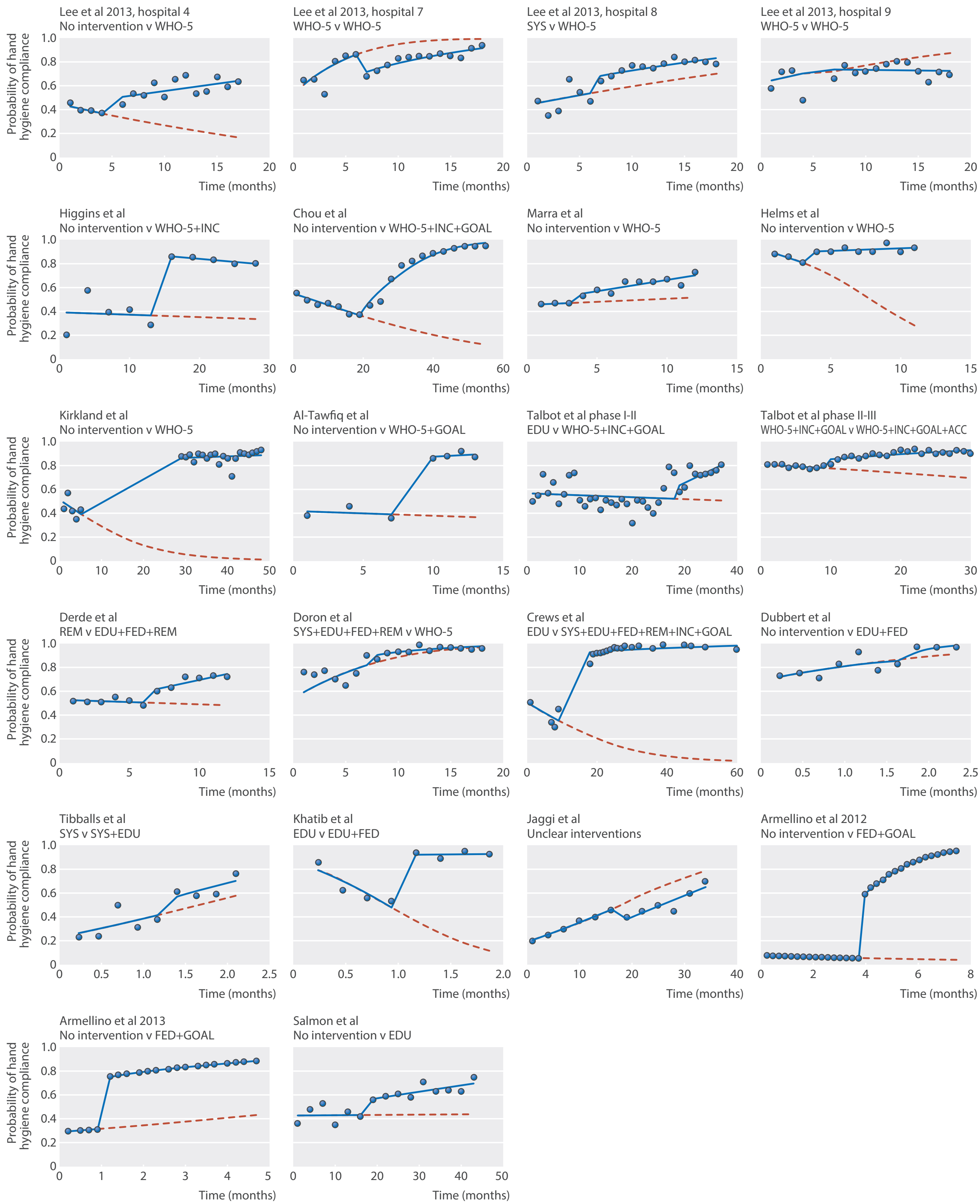


Fig 4 | **Re-analysis of studies involving interrupted time series where the outcome was hand hygiene compliance. Points represent observations, solid lines show expected values from fitted segmented regression models, and broken lines represent extrapolated trends before intervention. SYS=system change; EDU=education; FED=feedback; REM=reminders; SAF=institutional safety climate; INC=incentives; GOAL=goal setting; ACC=accountability; WHO-5=combined intervention strategies including SYS, EDU, FED, REM, and SAF**

Table 3 | Results of re-analysis of studies using interrupted time series to assess compliance with hand hygiene

		Baseline (intercept)					
Study	Comparison	% compliance	Coefficient (SE)	Coefficient (SE) for baseline trend	Coefficient (SE) for change in trend	Coefficient (SE) for change in level	Mean (95% CI)* % change in compliance
Lee[48]							
Hospital 4	No intervention *v* WHO-5	44.6	−0.215 (0.30)	−0.081 (0.10)	0.130 (0.10)	0.606 (0.26)	29.9 (3.5 to 56.4)
Hospital 7	WHO-5 *v* WHO-5	53.8	0.154 (0.29)	0.281 (0.07)	−0.151 (0.08)	−1.042 (0.25)	−11.5 (−13.5 to −9.5)
Hospital 8	SYS *v* WHO-5	44.6	−0.215 (0.26)	0.059 (0.06)	0.014 (0.06)	0.563 (0.19)	13.3 (−9.2 to 35.8)
Hospital 9	WHO-5 *v* WHO-5	62.3	0.503 (0.33)	0.088 (0.13)	−0.094 (0.13)	−0.007 (0.51)	−9.7 (−63.6 to 44.3)
Derde[42]	REM *v* EDU+FED+REM	52.8	0.112 (0.04)	−0.015 (0.01)	0.133 (0.02)	0.346 (0.05)	16.3 (13.6 to 19.1)
Higgins[45]	No intervention *v* WHO-5+INC	37.2	−0.428 (0.17)	−0.009 (0.25)	−0.030 (0.03)	2.448 (0.25)	48.8 (45.4 to 52.3)
Doron[43]	SYS+EDU+FED+REM *v* WHO-5	70.7	0.204 (0.12)	0.187 (0.10)	−0.040 (0.03)	0.586 (0.01)	4.7 (2.3 to 7.1)
Chou[40]†	No intervention *v* WHO-5+INC+GOAL	54.9	0.198 (0.03)	−0.039 (0.00)	0.151 (0.01)	0.453 (0.17)	56.4 (53.1 to 59.8)
Marra[50]	No intervention *v* WHO-5	45.7	−0.173 (0.07)	0.020 (0.06)	0.063 (0.03)	0.218 (0.06)	11.5 (3.4 to 19.6)
Helms[30]	No intervention *v* WHO-5	91.3	2.350 (0.42)	−0.297 (0.18)	0.354 (0.19)	0.706 (0.33)	35.9 (−5.8 to 77.7)
Kirkland[29]	No intervention *v* WHO-5	51.3	0.052 (0.14)	−0.097 (0.04)	0.111 (0.04)	4.443 (1.03)	83.3 (77.0 to 89.6)
Al-Tawfiq[28]	No intervention *v* WHO-5+GOAL	41.3	−0.350 (0.09)	−0.014 (0.02)	0.081 (0.07)	2.328 (0.21)	49.9 (42.8 to 57.0)
Crews[41]	EDU *v* SYS+EDU+FED+REM+INC+GOAL	50.7	0.028 (0.12)	−0.070 (0.02)	0.103 (0.02)	3.679 (0.22)	38.2 (35.5 to 40.9)
Talbot (phase I)[56]†	EDU *v* WHO-5+INC+GOAL	56.7	0.271 (0.20)	−0.006 (0.02)	0.109 (0.02)	0.363 (0.41)	18.5 (−1.4 to 38.4)
Talbot (phase II)[56]	WHO-5+INC+GOAL *v* WHO-5+INC+GOAL+ACC	81.1	1.455 (0.45)	−0.020 (0.01)	0.060 (0.01)	0.464 (0.05)	15.0 (10.6 to 19.5)
Dubbert[60]	No intervention *v* EDU+FED	69.5	0.822 (0.34)	0.636 (0.39)	2.908 (1.57)	−0.753 (0.75)	0.7 (−10.0 to 11.4)
Tibballs[65]	SYS *v* SYS+EDU	23.4	−1.186 (0.53)	0.187 (0.10)	−0.040 (0.03)	0.453 (0.57)	11.9 (−18.4 to 42.1)
Khatib[64]	EDU *v* EDU+FED	86.2	1.836 (0.17)	−2.051 (0.26)	2.185 (0.52)	2.549 (0.29)	65.8 (58.6 to 73.0)
Jaggi[46]	Unclear intervention details	19.5	−1.420 (0.26)	0.080 (0.02)	−0.006 (0.03)	−0.586 (0.34)	−14.8 (−33.1 to 3.6)
Armellino[38]†	No intervention *v* FED+GOAL	7.6	−2.493 (0.15)	−0.088 (0.133)	0.849 (0.235)	3.046 (0.68)	45.4 (38.5 to 52.3)
Armellino[37]†	No intervention *v* FED+GOAL	29.0	−0.895 (0.04)	0.122 (0.10)	−0.109 (0.08)	2.267 (0.14)	74.9 (65.5 to 84.4)
Salmon[54]‡	No intervention *v* EDU	42.7	−0.295 (0.17)	0.003 (0.02)	0.021 (0.02)	0.485 (0.22)	17.9 (−0.3 to 36.2)

SYS=system change; EDU=education; FED=feedback; REM=reminders; SAF=institutional safety climate; INC=incentives; GOAL=goal setting; ACC=accountability; WHO-5=combined intervention strategies including SYS, EDU, FED, REM, and SAF.
*Mean change in hand hygiene compliance during period after intervention period attributed to intervention accounting for baseline trends (see appendix 3 for details).
†Evidence of autocorrelation; Newey-West standard errors reported.
‡Hand hygiene compliance measured in student nurses.

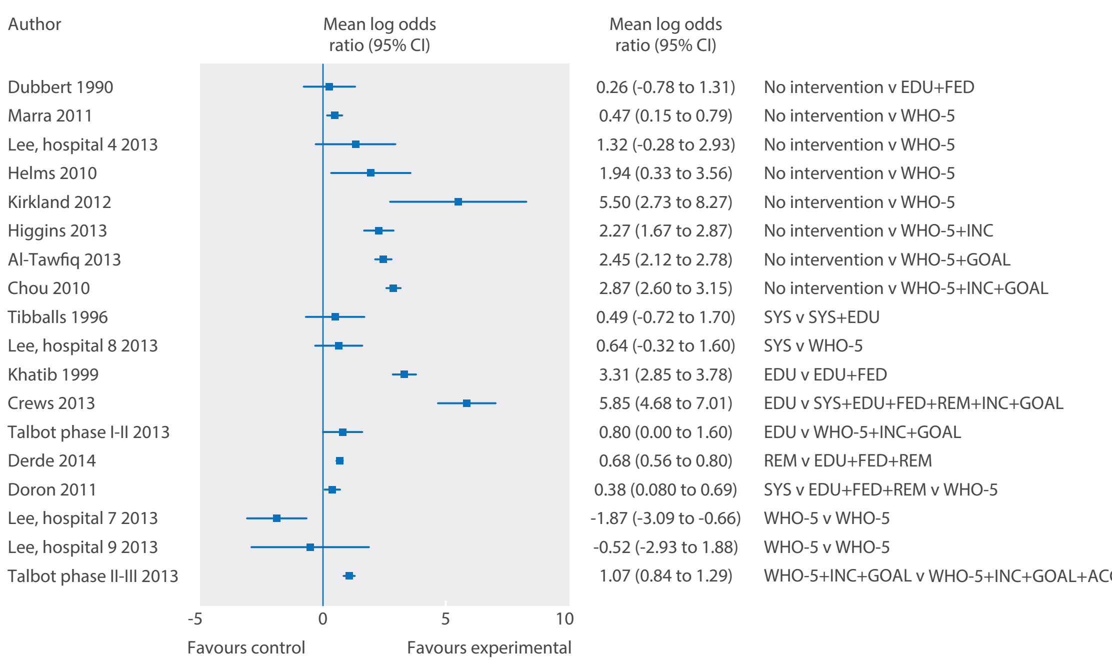


Fig 5 | Forest plot showing effect size as mean log odds ratios for hand hygiene compliance for all direct pairwise comparisons from interrupted time series studies. Lee and colleagues[48] was a multi-centre study. In hospitals 8 and 9 baseline strategy was already equivalent to WHO-5. SYS=system change; EDU=education; FED=feedback; REM=reminders; SAF=institutional safety climate; INC=incentives; GOAL=goal setting; ACC=accountability; WHO-5=combined intervention strategies including SYS, EDU, FED, REM, and SAF

doi: 10.1136/bmj.h3728 | *BMJ* 2015;351:h3728 | thebmj

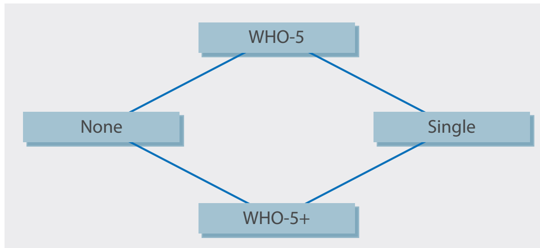


Fig 6 | **Network structure for network meta-analysis of four hand hygiene intervention strategies from interrupted time series studies. Intervention strategies were: none (no intervention); single intervention; WHO-5; and WHO-5+ (WHO-5 with incentives, goal-setting, or accountability)**

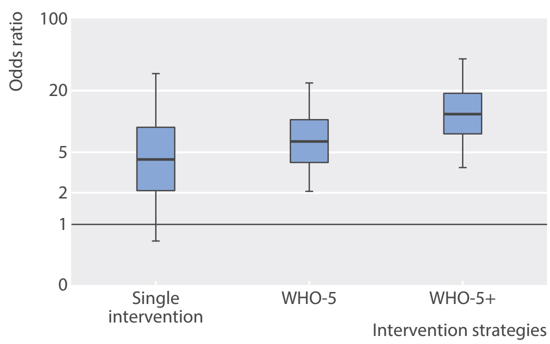


Fig 7 | **Box-and-whiskers plot showing relative efficacy of different hand hygiene intervention strategies compared with standard of care estimated by network meta-analysis from interrupted time series studies. Lower and upper edges represent 25th and 75th centiles from posterior distribution; central line median. Whiskers extend to 5th and 95th centiles. Intervention strategies were single intervention; WHO-5; and WHO-5+ (WHO-5 with incentives, goal-setting, or accountability). Appendix 9 shows results from sensitivity analysis that excluded studies where interventions were implemented as multiple time points**

hygiene, all components of the intervention were already in place in the baseline period.[48]

Twelve pairwise comparisons met the criteria for network meta-analysis, and included direct comparisons between all pairs of strategies except WHO-5 versus WHO-5+ and no intervention versus single intervention (fig 6). The network meta-analysis showed that although there was large uncertainty in effect sizes among the pairwise comparisons, point estimates for all intervention strategies indicated an improvement in compliance with hand hygiene compared with no intervention (fig 7). When two strategies, WHO-5 and WHO-5+, were compared with no intervention there was strong evidence that they were effective (table 2). The WHO5+ strategy also showed additional improvement compared with single intervention strategies and WHO-5 alone. For the latter comparison, which depended only on indirect comparisons, the estimated effect size was similar to that seen in the randomised controlled trials, though uncertainty was much larger (odds ratio for WHO-5 versus WHO-5+ was 1.82, 95% credible interval 0.2 to 12.2). WHO-5+ had the highest probability (67%) of being the best strategy in improving compliance (fig 8).

After we excluded studies with multiple stepwise interventions in the sensitivity analysis, there was a decrease in the effect size of all intervention strategies (appendix 4).

Clinical outcomes

Nineteen studies reported clinical or microbiological outcomes alongside hand hygiene outcomes. Six of these were multicentre studies,[35 42 48 55 62 67] and 13 were based in a single hospital.[28-30 46 47 49 52 56 57 59 63 66 69] All reported that improvements in hand hygiene were associated with reductions in at least one measure of hospital acquired infection and/or resistance rates. In most

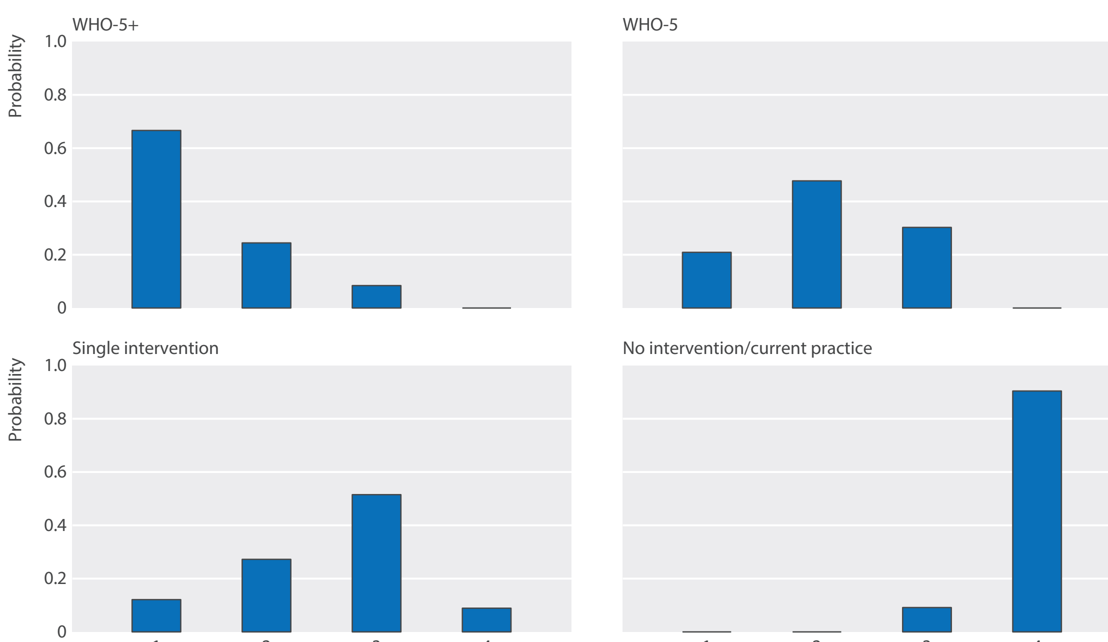


Fig 8 | **Rankograms showing probabilities of possible rankings for each intervention strategy (rank 1=best, rank 4=worst)**

case, however, either appropriate analysis was lacking, denominators were not reported, time series data were not shown (making interrupted time series designs vulnerable to pre-existing trends), or numbers were too small to draw firm conclusions.

There were, however, three single centre studies that did not have these limitations.[49 57 63] Two of these studies, which lasted about seven years, used time series analysis to study associations between use of alcohol hand rub and clinical outcomes, with adjustment for changing patterns of antibiotic use.[49 57] Lee and colleagues found strong evidence (P<0.001) that increased use of alcohol hand rub was associated with reduced incidence of healthcare associated infection and evidence that it was associated with reduced healthcare associated methicillin resistant *Staphylococcus aureus* (MRSA) infection (P=0.02).[49] Vernaz and colleagues found strong evidence that increased use of alcohol based hand rub was associated with reduced incidence of MRSA clinical isolates per 100 patient days (P<0.001), reporting that 1L of hand rub per 100 patient days was associated with a reduction in MRSA of 0.03 isolates per 100 patient days.[57] No association was found between increased use of alcohol based hand rub and clinical isolates of *Clostridium difficile*. Johnson and colleagues reported that an intervention in an Australian teaching hospital associated with a mean improvement of compliance with hand hygiene from 21% to 42% was also associated with declining trends in clinical MRSA isolates (by 36 months after the intervention clinical isolates per discharge had fallen by 40% compared with the baseline before the intervention), declining trends in MRSA bacteraemias (57% lower than baseline after 36 months), and declining trends in clinical isolates of extended spectrum β lactamases (ESBL) producing *E coli* and *Klebsiella* (>90% below baseline 36 months after intervention), though there was no evidence of changes in patient MRSA colonisation at four or 12 months after the intervention.[63] In addition to hand hygiene, however, the intervention included patient decolonisation and ward cleaning, and the relative importance of these measures cannot be determined.

Among the multicentre studies, Grayson and colleagues described a similar hand hygiene intervention (but without additional decolonisation or ward cleaning) initially introduced to six hospitals as a pilot study and, later, to 75 hospitals in Victoria, Australia, as part of a state-wide roll out.[62] Both the pilot and roll out were associated with large improvements in compliance (from about 20% to 50%) and similar clinically important trends after the intervention for reduced MRSA bacteraemias and MRSA clinical isolates per patient discharge (though in the state-wide roll out hospitals there was also a decline in MRSA clinical isolates before the intervention that continued after the intervention).

Roll out of a similar hand hygiene intervention (the Cleanyourhands campaign, based on WHO-5) in England and Wales was reported to be associated with reduced rates of MRSA bacteraemia (from 1.9 to 0.9 cases per 10 000 bed days) and *C difficile* infection (from 16.8 to 9.5 cases per 10 000 bed days), but no association was found with methicillin-sensitive *S aureus* (MSSA) bacteraemia.[55] This study also reported independent associations between procurement of alcohol hand rub and MRSA bacteraemias; in the last 12 months of the study, MRSA bacteraemias were estimated to have fallen by 1% (95% confidence interval 5% to 15%) for each additional mL of hand rub used per bed day (adjusted for other interventions and hospital level mupirocin use, a surrogate marker for MRSA screening and decolonisation). Similarly, each additional mL of soap used per bed day was associated with a 0.7% (0.4%, 1.0%) reduction in *C difficile* infection.

Benning and colleagues described the evaluation of a separate but contemporaneous patient safety intervention that included a hand hygiene component in nine English hospitals with nine matched controls.[67] Both intervention and control sites experienced large increases in consumption of soap and alcohol hand rub between 2004 and 2008 and substantial falls in rates of MRSA and *C difficile* infection, though in all cases (soap, hand rub, and infections) there was no evidence that differences between intervention and control sites resulted from anything other than chance.

In a two year study in 33 surgical wards in 10 European hospitals, Lee and colleagues found that, after adjustment for clustering, potential confounders, and temporal trends, enhanced hand hygiene alone was not associated with a reduction in MRSA clinical cultures and MRSA surgical site infections, and neither was a strategy of screening and decolonisation, but in wards where both interventions were combined, there was a reduction in the rate of MRSA clinical cultures of 12% per month (adjusted incidence rate ratio 0.88, 95% confidence interval 0.79 to 0.98).[48]

Among the randomised controlled trials, Mertz and colleagues found similar rates of hospital acquired MRSA colonisation in intervention and control groups (0.73 *v* 0.66 events per 1000 patient days, respectively; P=0.92), though adherence to hand hygiene was only 6% higher in the intervention arm.[35] Finally, in a study in 13 European intensive care units, Derde and colleagues reported a declining trend in acquisition of antimicrobial resistant bacteria (weekly incidence rate ratio 0.976, 95% confidence interval 0.954 to 0.999) associated with a hand hygiene intervention that increased compliance from about 50% to over 70%.[42] The decline was largely because of reduced MRSA acquisition. The intervention also included universal chlorhexidine body washing, and it is not possible to establish the relative importance of hand hygiene.

Level of information on resource use

Reporting of information on cost and resource use was limited, with 3, 26, and 12 studies classified as having high, moderate, and low information, respectively (appendix 8). Three studies reported costs associated with both materials and person time[34 52 66]; in two cases these reports were in separate papers.[70 71] Table 4 summarises the reported costs of interventions.

Table 4 | Extracted data on resource use in studies of interventions to improve hand hygiene in healthcare workers

Author (year), design	Intervention	Comparison	Settings and base year	Resource use: Materials	Resource use: Time	Sources	Total cost ($)*	No of beds	Intervention period (day)	Cost per 1000 bed day ($)
Huis (2013), CRCT	WHO-5 + goal-setting	WHO5 (except institutional safety climate)	Netherlands, 2009	State of art strategies: alcohol hand rub, website, leaflets, posters, newsletters, article in hospital magazines	State of art strategies: hand hygiene, direct observation. Extra time for performing hand hygiene	Separate paper[70]	320 278	993	365	883.7
				Team and leader directed strategies: as above	Team and leader directed strategies: as above plus coach salary, staffing costs for managers, role models and nurses in coaching session and preparation		474 068	1225	365	1060.5
Higgins (2013), ITS	WHO-5 + incentive	None (with AHR)	Ireland, 2010	Mobile interactive stand-alone computer using gaming technology and annual license. Swab and ATP machine	Research assistant for audit and training 1.79 FTE (287 hours) assuming salary as £2500 per month	Author contact	42 358	170	450	553.7
Armellino (2012), ITS	Feedback + goal-setting	None (unclear AHR use)	USA, 2008	21 video cameras	N/A	Paper	50 000	17	630	4668.5
Morgan (2012), ITS	System change + education + feedback + reminders	None (with AHR)	USA, 2010	60 alcohol dispensers system in two wards, 12 posters in total	1.46 FTE (234 hours) research assistants (10-20 hours/week for trouble shooting, refilling, and collecting data from devices, and 2 hours/month to design and present posters)	Author contact	6960	27	105	2455.0
Mestre (2012), ITS	Phase I: WHO-5. Phase II: WHO-5 (intense) + Reinforcement	Phase I: None (with AHR); phase II: WHO-5	Spain, 2011	Alcohol handrub solution. Material for campaign including posters, pens, and candy	Hand hygiene direct observation. Data analysis and interpretation	Separate paper[71]	19 259	n/a	365	385.2
Doron (2011), ITS	WHO-5	System change + education + feedback + reminders (with AHR)	USA, 2008-9	Cost for marketing consultancy	N/A	Author contact	35 000-50 000	425	365	225.6-322.3
Mayer (2011), NRT	Phase I: system change + education + feedback. Phase II: WHO-5 + incentive	None (unclear AHR use)	USA, 2003-6	Prizes as candy, chocolate bars, pizza, and others	2.25 FTE (yearly) of infection preventionists; 0.6 FTE of manager 0.35 FTE of clerk	Paper	165 600	450	365	1008.2

AHR=alcohol based hand rub, CRCT=cluster randomized controlled trial, ITS=interrupted time series, NRT= non-randomized trial, WHO-5=combined intervention including system change, education, feedback, reminders, and institution safety climate, N/A= not available, FTE=full time equivalents.
*$1=£0.65, €0.90.

Discussion

Principal findings

A multi-faceted hand hygiene intervention—WHO-5—and single interventions including system change, training and education, or reminders alone are associated with improved compliance with hand hygiene among healthcare workers in hospital compared with standard practice. Results from both randomised controlled trials and interrupted time series designs provide consistent evidence that adding supplemental interventions including goal setting, reward incentives, and accountability to the WHO-5 strategy lead to additional improvements in compliance. Information about resources used in the interventions was not well reported.

Comparison with other studies

We are aware of four previous systematic reviews of interventions for hand hygiene in healthcare settings.[5-8] One of these found only four studies of sufficient methodological quality to reliably evaluate interventions to promote hand hygiene and was unable to reach firm conclusions.[5] Overlap between included studies in the other three and our review is small: respectively four (9.8%),[8] three (7.3%),[6] and five (12.2%)[7] of studies included in our review were included in previous reviews, while 17 (80.1%), 38 (92.7%), and 40 (88.9%) of the studies in these reviews failed to meet the minimum quality threshold in ours.[12 13] While high quality non-randomised studies can potentially play an important role in the evaluation of interventions if they are analysed with appropriate methods, there are many reasons for thinking that simple before-after studies (a design used by most of the studies included in previous reviews) do not provide a reliable basis for evaluating interventions.[72-74] While an interrupted time series study (where multiple outcome measures are taken before and after the intervention) represents a strong quasi-experimental design, a before-after study compares a single outcome measure before and after the intervention and is vulnerable to distorting effects of pre-existing trends.

We found an increasing number of "high quality" studies on interventions for hand hygiene after 2009. From two previous systematic reviews[5 6] examining the literature from 1980 to November 2009, we found only 10 studies meeting the EPOC criteria (one randomised controlled trial, eight interrupted time series, and one controlled before-after study). With the same criteria, our review found 31 studies (five randomised controlled trials, 24 interrupted time series, one non-randomised trial, and one controlled before-after study) published between December 2009 and February 2014.

Reporting on resource implications for interventions was generally limited with some notable exceptions. Most included studies reported only part of the resources used, and methods for collecting cost data were unclear. Such information on resource use is important both for those wishing to implement similar strategies and for economic evaluation of different interventions.[10 75] A good framework to collect such data has also been proposed.[76] Cost effectiveness analysis of promotion of hand hygiene is required to assess under what circumstances these initiatives represent good value for money and when resources might be better directed at supplemental interventions, including care bundles,[77] ward cleaning,[78] and screening and decolonisation,[79] to complement well maintained compliance with hand hygiene.

Strengths and limitations of study

A particular strength of our study is that the network meta-analysis allowed us to quantify the relative efficacy among a series of different intervention strategies with different baseline interventions, even where the direct head-to-head comparisons were absent.

This study also has several limitations. Firstly, details on implementation of components of the intervention varied substantially. For example, personal feedback and group feedback were classified together, but, in practice, the impacts of these strategies can vary. Moreover, different studies might implement the same programme with different quality of delivery and level of adherence, so called intervention fidelity or type III error.[80] Both issues are common to many interventions to improve the quality of care in hospital settings and are likely to be responsible for much of the unexplained heterogeneity between studies.[81 82] Secondly, direct observation of compliance with hand hygiene might induce an increase in compliance unrelated to the intervention (the Hawthorne effect). Recent research suggests that such Hawthorne effects can lead to substantial overestimation of compliance.[83 84] Such effects, however, should not bias estimates of the relative efficacy of different interventions from randomised controlled trials and interrupted time series unless the effects vary between study arms/intervention periods. Thirdly, it is possible that it is the novelty of the intervention itself that leads to improvements in compliance and that any sufficiently novel intervention would do the same regardless of the components used. This clearly cannot be ruled out and is not necessarily inconsistent with our findings that interventions with more components tend to perform better. At present, however, there are too few high quality studies to evaluate whether individual components of interventions show consistent differences that cannot be explained by novelty alone. Fourth, results might be distorted by publication bias. Fifth, there might also be a low level of language bias because we excluded studies in languages other than English. The magnitude of such bias, however, is likely to be small.[85 86]

Finally, linking improved compliance to clinical outcomes such as number of infections prevented would provide more direct evidence about the value of such interventions.[10] Such direct evidence is still limited in hospital settings, although the association is supported by a growing body of indirect evidence as well as biological plausibility. Moreover, findings from studies included in our review that reported clinical or microbiological outcomes are consistent with substantial reductions in infections for some pathogens, such as MRSA, resulting from large improvements in hand hygiene.[87 88] The lack of a measureable effect of improved hand hygiene on MSSA infections might seem paradoxical but can be partly explained by the fact that MSSA infections are much more likely to be of endogenous origin, whereas MRSA is more often linked to nosocomial cross transmission. Moreover, predictions from modelling studies that hand hygiene will have a disproportionate effect on the prevalence of resistant bacteria in hospitals (provided resistance is rare in the community) seem to have been borne out in practice.[89]

Conclusions

While there is some evidence that single component interventions lead to improvements in hand hygiene, there is strong evidence that the WHO-5 intervention can lead to substantial, rapid, and sustained improvements in compliance with hand hygiene among healthcare workers in hospital settings. There is also evidence that goal setting, reward incentives, and accountability provide additional improvements beyond those achieved by WHO-5. Important directions for future work are to improve reporting on resource implications for interventions, increasingly focus on strong study designs, and evaluate the long term sustainability and cost effectiveness of improvements in hand hygiene.

We are grateful to all authors of the literature included in this review who responded to requests for additional information. We also thank the infection control staff of Sappasithiprasong Hospital for technical support and Cecelia Favede for help in editing.

Contributors: NL, BSC, YL, DL, NG, and ND contributed to the study conception and design. NL and BSC extracted data, and NL performed the data analysis. NL wrote the first draft. DL, YL, MH, ASL, SH, NG, ND, and BSC critically revised the manuscript for important intellectual content. All authors read and approved the final manuscript. NL and BSC are guarantors.

Funding: This research was part of the Wellcome Trust-Mahidol University-Oxford Tropical Medicine Research Programme supported by the Wellcome Trust of Great Britain (089275/Z/09/Z). BSC was supported by the Oak Foundation and the Medical Research Council and Department for International Development (grant No MR/K006924/1).

Competing interests: All authors have completed the ICMJE uniform disclosure form at http://www.icmje.org/coi_disclosure.pdf and declare: no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Ethical approval: Not required

Data sharing: The relevant data and code used in this study are available from the authors.

Transparency: The lead author affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

1 Weinstein RA. Nosocomial infection update. *Emerg Infect Dis* 1998;4:416-20.
2 Jarvis WR. Selected aspects of the socioeconomic impact of nosocomial infections: morbidity, mortality, cost, and prevention. *Infect Control Hosp Epidemiol* 1996;17:552-7.
3 Rosenthal VD, Maki DG, Jamulitrat S, et al. International Nosocomial Infection Control Consortium (INICC) report, data summary for 2003-2008, issued June 2009. *Am J Infect Control* 2010;38:95-104.e2

4 WHO guidelines on hand hygiene in health care (First global patient safety challenge clean care is safer care). WHO, 2009.
5 Gould DJ, Moralejo D, Drey N, Chudleigh JH, Interventions to improve hand hygiene compliance in patient care. *Cochrane Database Syst Rev* 2011:9:CD005186.
6 Huis A, van Achterberg T, de Bruin M, et al. A systematic review of hand hygiene improvement strategies: a behavioural approach. *Implement Sci* 2012;7:92.
7 Schweizer ML, Reisinger HS, Ohl M, et al. Searching for an optimal hand hygiene bundle: a meta-analysis. *Clin Infect Dis* 2014;58:248-59.
8 Naikoba S, Hayeard A. The effectiveness of interventions aimed at increasing handwashing in healthcare workers—a systematic review. *J Hosp Infect* 2001;47:173-80.
9 Drummond MF, Sculpher MJ, Torrance GW, O'Brien BJ, Stoddart GL. Methods for the economic evaluation of health care programmes. Oxford University Press, 2005.
10 Graves N, Halton K, Page K, Barnett A. Linking scientific evidence and decision making: a case study of hand hygiene interventions. *Infect Control Hosp Epidemiol* 2013;34:424-9.
11 Moher D, Liberati A, Tetzlaff J, Altman DG. The PRISMA Group (2009) preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009;6:e1000097.
12 Effective Practice and Organisation of Care (EPOC). What study designs should be included in an EPOC review? EPOC Resources for review authors. Norwegian Knowledge Centre for the Health Services; 2013. http://epoc.cochrane.org/epoc-specific-resources-review-authors.
13 Cochrane Effective Practice and Organisation of Care Review Group. Data Collection Checklist. EPOC Resources for review authors. Norwegian Knowledge Centre for the Health Services; 2013. http://epoc.cochrane.org/sites/epoc.cochrane.org/files/uploads/datacollectionchecklist.pdf.
14 Higgins JPT, Green S. Cochrane handbook for systematic reviews of interventions. Version 5.1.0 [updated March 2011]. The Cochrane Collaboration 2011. www.cochrane-handbook.org.
15 DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986;7:177-88.
16 Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. Identifying and quantifying heterogeneity. Part 4: Heterogeneity. In: Introduction to meta-analysis. John Wiley, 2009:107-25.
17 Peters JL, Sutton AJ, Jones DR, Abrams KR, Rushton L. Contour-enhanced meta-analysis funnel plots help distinguish publication bias from other causes of asymmetry. *J Clin Epidemiol* 2008;61:991-6.
18 Taljaard M, McKenzie JE, Ramsay CR, Grimshaw JM. The use of segmented regression in analysing interrupted time series studies: an example in pre-hospital ambulance care. *Implement Sci* 2014;9:77.
19 Ramsay CR, Matowe L, Grilli R, Grimshaw JM, Thomas RE. Interrupted timeseries designs in health technology assessment: lessons from two systematic reviews of behavior change strategies. *Int J Technol Assess Health Care* 2003;19:613-23.
20 Vidanapathirana J, Abramson M, Forbes A, Fairley C. Mass media interventions for promoting HIV testing. *Cochrane Database Syst Rev* 2005;3:CD004775.
21 Newey WK, West KD. A simple, positive semi-definite, heteroskedasticity and autocorrelation consistent covariance matrix. *Econometrica* 1987;55:703-8.
22 Bolker BM. Ecological models and data in R. Princeton University Press, 2008.
23 R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing, 2014. www.R-project.org/.
24 Lu G, Ades AE. Combination of direct and indirect evidence in mixed treatment comparisons. *Stat Med* 2004;23:3105-24.
25 Sutton A, Ades AE, Cooper N, Abrams K. Use of indirect and mixed treatment comparisons for technology assessment. *Pharmacoeconomics* 2008;26:753-67.
26 Spiegelhalter DJ, Thomas A, Best N, Lunn D. WinBUGS user manual. Version 1.4 January 2003. www.mrc-bsu.cam.ac.uk/bugs.
27 Dias S, Welton NJ, Caldwell DM, Ades AE. Checking consistency in mixed treatment comparison meta-analysis. *Stat Med* 2010;29:932-44.
28 Al-Tawfiq JA, Abed MS, Al-Yami N. Promoting and sustaining a hospital-wide, multifaceted hand hygiene program resulted in significant reduction in health care-associated infections. *Am J Infect Control* 2013;41:482-6
29 Kirkland KB, Homa KA, Lasky RA, et al. Impact of a hospital-wide hand hygiene initiative on healthcare-associated infections: results of an interrupted time series. *BMJ Qual Saf* 2012;21:1019-26.
30 Helms B, Dorval S, Laurent P, Winter M. Improving hand hygiene compliance: a multidisciplinary approach. *Am J Infect Control* 2010;38:572-4.
31 Fisher DA, Seetoh T, Oh May-Lin H, et al. Automated measures of hand hygiene compliance among healthcare workers using ultrasound: validation and a randomized controlled trial. *Infect Control Hosp Epidemiol* 2013;34:919-28.
32 Fuller C, Michie S, Savage J, et al. The Feedback Intervention Trial (FIT)—improving hand-hygiene compliance in UK healthcare workers: a stepped wedge cluster randomised controlled trial. *PLoS ONE* 2012;7:e41617.
33 Huang J, Jiang D, Wang X, et al. Changing knowledge, behavior, and practice related to universal precautions among hospital nurses in China. *J Contin Educ Nurs* 2002;33:217-24.
34 Huis A, Schoonhoven L, Grol R, et al. Impact of a team and leaders-directed strategy to improve nurses' adherence to hand hygiene guidelines: a cluster randomised trial. *Int J Nurs Stud* 2013;50:464-74.
35 Mertz D, Dafoe N, Walter SD, Brazil K, Loeb M. Effect of a multifaceted intervention on adherence to hand hygiene among healthcare workers: a cluster-randomized trial. *Infect Control Hosp Epidemiol* 2010;31:1170-6.
36 Salamati P, Poursharifi H, Rahbarimanesh AA, Koochak HE, Najfi Z. Effectiveness of motivational interviewing in promoting hand hygiene of nursing personnel. *Int J Prev Med* 2013;4:441-7.
37 Armellino D, Trivedi M, Law I, et al. Replicating changes in hand hygiene in a surgical intensive care unit with remote video auditing and feedback. *Am J Infect Control* 2013;41:925-7.
38 Armellino D, Hussian E, Schilling ME, et al. Using high-technology to enforce low-technology safety measures: the use of third-party remote video auditing and real-time feedback in healthcare. *Clin Infect Dis* 2012;54:1-7.
39 Chan BP, Homa K, Kirkland KB. Effect of varying the number and location of alcohol-based hand rub dispensers on usage in a general inpatient medical unit. *Infect Control Hosp Epidemiol* 2013;34:987-9.
40 Chou T, Kerridge J, Kulkarni M, Wickman K, Malow J. Changing the culture of hand hygiene compliance using a bundle that includes a violation letter. *Am J Infect Control* 2010;38:575-8.
41 Crews JD, Whaley E, Syblik D, Starke J. Sustained improvement in hand hygiene at a children's hospital. *Infect Control Hosp Epidemiol* 2013;34:751-3.
42 Derde LPG, Cooper BS, Goossens H, et al. Interventions to reduce colonisation and transmission of antimicrobial-resistant bacteria in intensive care units: an interrupted time series study and cluster randomised trial. *Lancet Infect Dis* 2014;14:31-9.
43 Doron SI, Kifuji K, Hynes BT, et al. A multifaceted approach to education, observation, and feedback in a successful hand hygiene campaign. *Jt Comm J Qual Patient Saf* 2011;37:3-10.
44 Helder OK, Weggelaar AM, Waarsenburg DCJ, et al. Computer screen saver hand hygiene information curbs a negative trend in hand hygiene behavior. *Am J Infect Control* 2012;40:951-4.
45 Higgins A, Hannan M. Improved hand hygiene technique and compliance in healthcare workers using gaming technology. *J Hosp Infect* 2013;84:32-7.
46 Jaggi N, Sissodia P. Multimodal supervision programme to reduce catheter associated urinary tract infections and its analysis to enable focus on labour and cost effective infection control measures in a tertiary care hospital in India. *J Clin Diagn Res* 2012;6:1372-6.
47 Koff MD, Corwin HL, Beach ML, Surgenor SD, Loftus RW. Reduction in ventilator associated pneumonia in a mixed intensive care unit after initiation of a novel hand hygiene program. *J Crit Care* 2011;26:489-95.
48 Lee AS, Cooper BS, Malhotra-Kumar S, et al. Comparison of strategies to reduce meticillin-resistant Staphylococcus aureus rates in surgical patients: a controlled multicentre intervention trial. *BMJ Open* 2013;3:e003126.
49 Lee YT, Chen SC, Lee MC, et al. Time-series analysis of the relationship of antimicrobial use and hand hygiene promotion with the incidence of healthcare-associated infections. *J Antibiot (Tokyo)* 2012;65:311-6.
50 Marra AR, Noritomi DT, Westheimer Cavalcante AJ, et al. A multicenter study using positive deviance for improving hand hygiene compliance. *Am J Infect Control* 2013;41:984-8.
51 Marra AR, Guastelli LR, de Araújo CM, et al. Positive deviance: a program for sustained improvement in hand hygiene compliance. *Am J Infect Control* 2011;39:1-5.
52 Mestre G, Berbel C, Tortajada P, et al. "The 3/3 strategy": a successful multifaceted hospital wide hand hygiene intervention based on WHO and continuous quality improvement methodology. *PLoS One* 2012;7:e47200.
53 Morgan DJ, Pineles L, Shardell M, et al. Automated hand hygiene count devices may better measure compliance than human observation. *Am J InfectControl* 2012;40:955-9.
54 Salmon S, Wang XB, Seetoh T, Lee SY, Fisher DA. A novel approach to improve hand hygiene compliance of student nurses. *Antimicrob Resist Infect Control* 2013;2:16.
55 Stone SP, Fuller C, Savage J, et al. Evaluation of the national Cleanyourhands campaign to reduce Staphylococcus aureus bacteraemia and Clostridium difficile infection in hospitals in England and Wales by improved hand hygiene: four year, prospective, ecological, interrupted time series study. *BMJ* 2012;344:e3005.
56 Talbot TR, Johnson JG, Fergus C, et al. Sustained improvement in hand hygiene adherence: utilizing shared accountability and financial incentives. *Infect Control Hosp Epidemiol* 2013;34:1129-36.

57 Vernaz N, Sax H, Pittet D, et al. Temporal effects of antibiotic use and hand rub consumption on the incidence of MRSA and Clostridium difficile. *J Antimicrob Chemother* 2008;62:601-7.
58 Whitby M, McLaws ML, Slater K, Tong E, Johnson B. Three successful interventions in health care workers that improve compliance with hand hygiene: is sustained replication possible? *Am J Infect Control* 2008;36:349-55.
59 Yngstrom D, Lindstrom K, Nystrom K, et al. Healthcare-associated infections must stop: a breakthrough project aimed at reducing healthcare-associated infections in an intensive-care unit. *BMJ Qual Saf* 2011;20:631-6.
60 Dubbert PM, Dolce J, Richter W, Miller M, Chapman SW. Increasing ICU staff handwashing: effects of education and group feedback. *Infect Control Hosp Epidemiol* 1990;11:191-3.
61 Eldridge NE, Wood SS, Bonello RS, et al. Using the six sigma process to implement the Centers for Disease Control and Prevention guideline for hand hygiene in 4 intensive care units. *J Gen Intern Med* 2006;21(suppl 2):S35-42.
62 Grayson ML, Jarvie LJ, Martin R, et al. Significant reductions in methicillin-resistant Staphylococcus aureus bacteraemia and clinical isolates associated with a multisite, hand hygiene culture-change program and subsequent successful statewide roll-out. *Med J Aust* 2008;2;188:633-40.
63 Johnson PD, Martin R, Burrell LJ, et al. Efficacy of an alcohol/chlorhexidine hand hygiene program in a hospital with high rates of nosocomial methicillin-resistant Staphylococcus aureus (MRSA) infection. *Med J Aust* 2005;183:509-14.
64 Khatib M, Jamaleddine G, Abdallah A, Ibrahim Y. Hand washing and use of gloves while managing patients receiving mechanical ventilation in the ICU. *Chest* 1999;116:172-5.
65 Tibballs J. Teaching hospital medical staff to handwash. *Med J Aust* 1996;164:395-8.
66 Mayer J, Mooney B, Gundlapalli A, et al. Dissemination and sustainability of a hospital-wide hand hygiene program emphasizing positive reinforcement. *Infect Control Hosp Epidemiol* 2011;32:59-66.
67 Benning A, Dixon-Woods M, Nwulu U, et al. Multiple component patient safety intervention in English hospitals: controlled evaluation of second phase. *BMJ* 2011;342:d199.
68 Gould D, Chamberlain A. The use of a ward-based educational teaching package to enhance nurses' compliance with infection control procedures. *J Clin Nurs* 1997;6:55-67.
69 Marra AR, Guastelli LR, de Araújo CM, et al. Positive deviance: a new strategy for improving hand hygiene compliance. *Infect Control Hosp Epidemiol* 2010;31:12-20.
70 Huis A, Hulscher M, Adang E, et al. Cost-effectiveness of a team and leaders-directed strategy to improve nurses' adherence to hand hygiene guidelines: a cluster randomised trial. *Int J Nurs Stud* 2013;50:518-26.
71 Mestre G, Berbel G, Tortajada P, et al. Monitoratge periòdic, retroacció immediata i treball en equip: claus de l'èxit i sostenibilitat de l'estratègia 3/3 d'higiene de mans. *Annals de Medicina* 2013;96:1-7.
72 Ansari F, Grey K, Nathwani D, et al. Outcomes of an intervention to improve hospital antibiotic prescribing: interrupted time series with segmented regression analysis. *J Antimicrob Chemother* 2003;52:842-8.
73 Davey P, Brown E, Charani E, et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. *Cochrane Database Syst Rev* 2013;30:CD003543.
74 Marwick CA, Guthrie B, Pringle JEC, et al. A multifaceted intervention to improve sepsis management in general hospital wards with evaluation using segmented regression of interrupted time series. *BMJ Qual Saf* 2014;23:e2.
75 Graves N, Halton K, Lairson D. Economics and preventing hospital-acquired infection: broadening the perspective. *Infect Control Hosp Epidemiol* 2007;28:178-84.
76 Page K, Graves N, Halton K, Barnett AG. Humans, "things" and space: costing hospital infection control interventions. *J Hosp Infect* 2013;84:200-5.
77 Aboelela SW, Stone PW, Larson EL. Effectiveness of bundled behavioural interventions to control healthcare-associated infections: a systematic review of the literature. *J Hosp Infect* 2007;66:101-8.
78 Dancer SJ. Mopping up hospital infection. *J Hosp Infect* 1999;43:85100.
79 Harbarth S, Fankhauser C, Schrenzel J, et al. Universal screening for methicillin-resistant Staphylococcus aureus at hospital admission and nosocomial infection in surgical patients. *JAMA* 2008;299:1149-57.
80 Carroll C, Patterson M, Wood S, et al. A conceptual framework for implementation fidelity. *Implement Sci* 2007;30:40.
81 Dijkstra R, Wensing M, Thomas R, et al. The relationship between organisational characteristics and the effects of clinical guidelines on medical performance in hospitals, a meta-analysis. *BMC Health Serv Res* 2006;28:53.
82 Turner RM, Spiegelhalter DJ, Smith GC, Thompson SG. Bias modelling in evidence synthesis. *J R Stat Soc Ser A Stat Soc* 2009;172:21-47.
83 Hagel S, Reischke J, Kesselmeier M, et al. Quantifying the Hawthorne Effect in hand hygiene compliance through comparing direct observation with automated hand hygiene monitoring. *Infect Control Hosp Epidemiol* 2015;Apr 23:1-6.
84 Srigley JA, Furness CD, Baker GR, Gardam M. Quantification of the Hawthorne effect in hand hygiene compliance monitoring using an electronic monitoring system: a retrospective cohort study. *BMJ Qual Saf* 2014;23:974-80.
85 Jüni P, Holenstein F, Sterne J, Bartlett C, Egger M. Direction and impact of language bias in meta-analyses of controlled trials: empirical study. *Int J Epidemiol* 2002;31:115-23.
86 Morrison A, Polisena J, Husereau D, et al. The effect of English-language restriction on systematic review-based meta-analyses: a systematic review of empirical studies. *Int J Technol Assess Health Care* 2012;28:138-44.
87 Bauer TM, Ofner E, Just HM, Just H, Daschner F. An epidemiological study assessing the relative importance of airborne and direct contact transmission of microorganisms in a medical intensive care unit. *J Hosp Infect* 1990;15:301-9.
88 Hugonnet S, Pittet D. Hand hygiene-beliefs or science? *Clin Microbiol Infect* 2000;6:350-6.
89 Lipsitch M, Bergstrom CT, Levin BR. The epidemiology of antibiotic resistance in hospitals: paradoxes and prescriptions. *Proc Natl Acad Sci USA* 2000;97:1938-43.

Appendix 1: Complete search strategy
Appendix 2: Classification for level of information on resources use
Appendix 3: Analysis of interrupted time series data
Appendix 4: WINBUGs code for network meta-analysis
Appendix 5: Excluded studies with reason by EPOC criteria
Appendix 6: Details of included studies
Appendix 7: Funnels plots figs A-D
Appendix 8: Details of extracted intervention components and level of information on resource use
Appendix 9: Supplementary results from sensitivity analysis